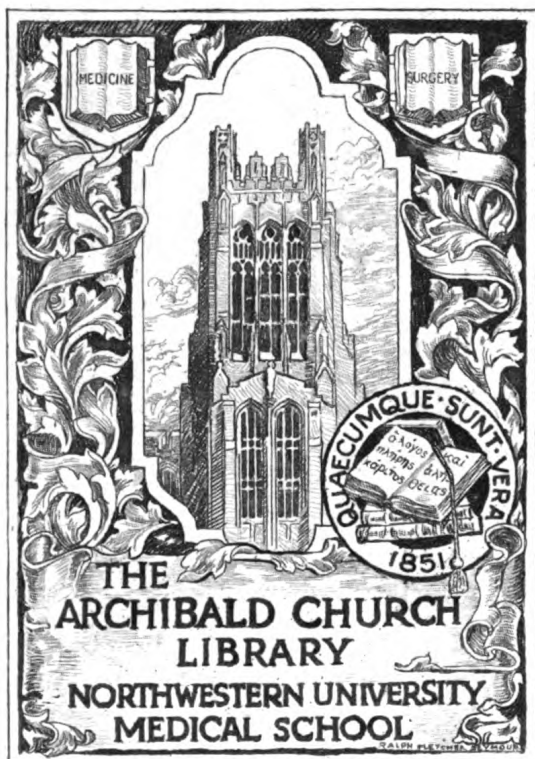


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THE PATHOLOGICAL LABORATORY

LONDON COUNTY ASYLUMS
CLAYBURY ESSEX

VOL. VI.



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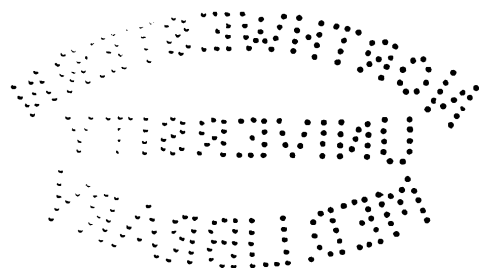
EDITED BY
FREDERICK WALKER MOTT, M.D., F.R.S., F.R.C.P.,
*Director of the Laboratory and Pathologist to the London County Asylums;
Consulting Physician to Charing Cross Hospital;
Consulting Physician to the Queen Alexandra Military Hospital;
Corresponding Member of the Société de Psychiatrie de Paris.*

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PREFACE.

In the five preceding volumes of the Archives of Neurology and Psychiatry considerable attention has been devoted to the causal connection of syphilis to general paralysis of the insane. In the first volume published a few years after my appointment, I called attention to the fact that syphilis was either not mentioned or hardly mentioned as a cause of mental disease in the reports. Thus I stated in the preface: "If a comparison be made between the number of new cases attributable to syphilis in the reports of 1897 and 1898 at Claybury it may be gathered that in the later years more interest and attention had been devoted to the subject, for out of a total of 958 patients admitted in 1896 in three the probable cause of insanity is noted to be venereal disease; while out of a total of 678 admitted in 1897 it is 40." This increase was mainly due to the interest taken at my suggestion on this question by one of the medical officers.

The links in the chain of circumstantial evidence which showed that if there were no syphilis there would be no general paralysis are as follows:—(1) A history of syphilitic affection usually of a mild form as regards secondary and tertiary symptoms can be obtained in as large a proportion of cases of general paralysis as in obvious syphilitic skin lesions. (2) A correlation of the incidence of syphilis and the incidence of general paralysis occurs in the two sexes according to the social grade. (3) In 60 cases of the juvenile form of general paralysis I have found evidence of congenital syphilis either in the family history, or by signs on the body of the patient in nearly every instance and in not one could it be excluded. Mental stress, alcoholism and sexual excesses, the previously attributed causes of general paralysis in the adult can in these cases be excluded. (4) I have shown that Fournier was right in asserting that tabes dorsalis and general paralysis are pathogenetically one and the same disease affecting different parts of the nervous system, for I collected 70 cases of tabo-paralysis and 70 cases of tabes dorsalis, and I found that some began as tabes and ended in general paralysis; in others the spinal and cerebral symptoms started simultaneously; while again in others, it began with optic atrophy and ended in spinal tabes or tabo-paralysis. The average time for symptoms to arise after the infection is the same, viz., 10 to

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15 years. (5) In all my very large experience I have never seen a primary sore or secondary rash on a general paralytic in spite of the fact that many of them must have laid themselves open to infection, and Krafft-Ebing observing the same fact showed that paralytics were incapable of reinfection.

This chain of circumstantial evidence was strong enough for most neurologists, but it did not satisfy the majority of alienists in this country; still circumstantial evidence is the best of evidence if no link in the chain is missing and each link is a good one. Direct observation and experiment must, however, be the final test.

The discovery of the *Spirochaeta pallida* by Schaudinn and the successful inoculation of anthropoid apes by Hoffmann, Metchnikoff, Neisser and others, which was extended to other animals such as apes and rabbits, showed that syphilis was due to a living organism; the inference may therefore be drawn that the reason why paralytics are not capable of reinfection is that the organism is still in the body.

The introduction of the Wassermann reaction which demonstrates antecedent syphilis added a new and important link to the chain of evidence, for it has been found by Plaut and confirmed by Candler, Henderson Smith, and Mann that practically every case of general paralysis gives a positive reaction not only of the blood but also of the cerebrospinal fluid.

There still remained many alienists who doubted that syphilis was the essential cause of general paralysis. The epoch-making discovery of Noguchi and Moore of the *Spirochaeta pallida* in 12 out of 70 brains of general paralytics forged the last and strongest link, viz., that of direct observation. Noguchi extended his observations and found the organism in twenty-five per cent. of cases. I have, in the Laboratory, been able in a large series of cases to demonstrate the existence of the specific organism in sixty-six per cent. Sometimes they can be found in ten minutes, sometimes only after a day's search, but inasmuch as looking for these minute organisms in a large organ like the brain may be like looking for the proverbial needle in a hay stack, it is not surprising they cannot be found in every case. The existence of the positive Wassermann reaction in the cerebrospinal fluid in every case, however, strongly supports this conclusion.

Fifteen per cent. of the male admissions to the London County Asylums are general paralytics, and seeing that these patients prior to the disease are in the prime of life and able individuals in body and mind and no matter from what social grade they come are usually of civic worth, and, as a rule, not possessed of a neuropathic inheritance, it follows, that now we have a precise knowledge of the cause of this terrible malady the State should make every endeavour to prevent it and failing that to cure it. When we reflect that

last year £600,000 was spent by the Asylums Committee of the London County Council alone in the maintenance of lunatics, would it not be an advantage to the State if a fraction of this immense sum of money were, in the future, devoted to the prevention of this widespread and potent cause of one of the worst forms of mental disease?

If it were possible to adopt such preventive measures as would diminish the number of individuals infected with syphilis the number of admissions to asylums of cases of general paralysis would proportionately diminish. The effect, however, would not be felt for years owing to its being a late manifestation. Recent published statistics in Vienna show that of 4,134 officers infected, 198 subsequently suffered with general paralysis, 116 of locomotor ataxy, and 134 of cerebrospinal syphilis. But this is only a part of the toll, for it is known that syphilis is a potent cause in the production of blindness, deafness, imbecility, idiocy, aneurism and arterial disease; moreover, it lowers the vital resistance to other infections, such as tubercle. Again, all measures which led to the prevention of the spread of syphilis, so prevalent in our large cities, would greatly increase the birth-rate of healthy children, for syphilis of the parents, especially when the mother is infected, is a frequent cause of miscarriages, abortions, still-births and children dying in early infancy of marasmus, hydrocephalus, convulsions and meningitis.

The discovery of the specific organism and the blood test have shed a new light on this racial plague, culminating in the discovery by Ehrlich of a new means of treatment of this disease. In all civilised countries this treatment by injections of salvarsan or neo-salvarsan has met with the greatest success. The experience of Colonel Gibbard and Major Harrison at the Military Hospital, Rochester Row, of intravenous injection of salvarsan immediately the primary infection is discovered by microscopic demonstration of the spirochaete, and before it has become generalised in the body, leads to the hope that by this early treatment followed by mercurial injections, not only the spread of infection may in great measure be averted, but the late manifestations of the disease above mentioned be certainly greatly diminished.

It might be said that a great many cases of general paralysis and tabes occur in spite of a prolonged and thorough course of mercurial treatment. It may be so, but it all depends upon when the course of treatment was commenced. It is known that the primary sore in these cases so often resembles a soft (non-syphilitic) sore that treatment was not commenced until secondary symptoms had occurred, and then a prolonged mercurial treatment was adopted. It is quite probable that the treatment was then too late to prevent sowing of the specific organism in the central nervous system. It has been

shown that lumbar puncture, when the roseolar rash appears frequently reveals a lymphocytosis of the cerebrospinal fluid indicative of specific infection, although the clinical symptoms may have been so mild as to have escaped notice. Time and scientific investigation alone will show whether this premise is true. From an economic point of view alone, it would amply repay the State to promote measures whereby all classes would be able to obtain the earliest diagnosis and adequate treatment.

The study of the neuropathic inheritance is one which was commenced five years ago and is already bearing fruit. I wished to learn if the convolitional pattern of the brain like the physiognomy was inherited and I instituted a card system of relatives with the object of obtaining the brains of persons, nearly related, dying in the London County Asylums. Dr. Edgar Schuster was kind enough to offer his services in the description of the folds and fissures of brains of relatives in accordance with the admirable plan he adopted in describing three "Chinese Brains" now in the Museum of the Royal College of Surgeons. His paper on the "Hereditary Resemblance in the Fissures of the Cerebral Hemispheres" is an extremely accurate and careful description of the brains of a mother and daughter and of two brothers. There is also by the same author an excellent description of the convolitional pattern of the "Brain of a Malay."

There are several papers on the neuropathic inheritance in relation to insanity based upon the statistics afforded by the cards of 3,500 relatives who are at present or who have been in the London County Asylums, together with interesting investigations by carefully recorded pedigrees. The paper by Dr. Wilson White referring to 25 pedigrees of insane persons is especially valuable; likewise the carefully recorded pedigrees of Dr. Wootton.

Previous volumes of the Archives of the Laboratory have contained many papers on comparative neuro-biology, and this is no exception, as there is a long and carefully exact description of the cortical cell lamination of the hemispheres of some rodents by Dr. Droogleever Fortuyn.

Lastly may be mentioned the thesis by Dr. Baines "Notes on the Etiology, Pathology and Clinical Aspects of Cases of Insanity Occurring in the Involutional Period of Life." This concludes the new work, but in the Appendix are a number of papers which have appeared in the Proceedings of the Royal Society of Medicine by various workers in the Laboratory, also a paper on "The Relation of Head Injury to Nervous and Mental Disease," which formed the subject of my address at the opening of a discussion on this subject at the British Medical Association held at Birmingham in 1911; it also appeared by request in the Transactions of the Australasian Congress of Medicine of the same year.

When the next number of the Archives appears it is probable the Maudsley Hospital and the Pathological department, its staff and equipments at Denmark Hill, will be in active operation. It is hoped that the facilities which will then be afforded for a clinical and laboratory research on a small number of cases of different types of insanity in the early and yet curable stage may throw new light on the essential causes and contributory factors which lead to mental disorder and derangement. It is only by such means that we can hope either to prevent or cure mental disease.

In conclusion, I wish to express my indebtedness to my assistant Mr. Sydney A. Mann for much help in revising the proofs and arranging many details, also to my assistant Mr. Charles Geary for his technical skill and assistance in photomicrography and histology.

FREDERICK W. MOTT.

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- (1) The Relation of Head Injury to Nervous and Mental Disease, by F. W. Mott, M.D., F.R.S., F.R.C.P.
- (2) Is Insanity on the Increase ? by F. W. Mott, M.D., F.R.S., F.R.C.P.
(Reprinted from the "Sociological Review," vol. vi, No. 1.)
- (3) Microscopical Investigation of the Nervous System in Three Cases of Spontaneous Myxoedema, by R. Brun, M.D., and F. W. Mott, M.D., F.R.S., F.R.C.P.
(Reprinted from the "Proceedings of the Royal Society of Medicine," 1913, vol. vi.)
- (4) Fatal Pellagra in Two English Boys, with the Results of the Pathological Investigation of One Case, by Charles R. Box, M.D., and F. W. Mott, M.D., F.R.S., F.R.C.P.
(Reprinted from the "Transactions of the Society of Tropical Medicine and Hygiene," April, 1913.)
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- (6) The Complete Histo-pathological Examination of the Nervous System of an Unusual Case of Obstetrical Paralysis Forty-One Years after Birth, and a Review of the Pathology, by Geo. F. Boyer, M.B. (Toronto).
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- (7) The Changes in the Central Nervous System resulting from Thyro-parathyroidectomy, by Walter Edmunds, F.R.C.S.
(Reprinted from the "Proceedings of the Royal Society of Medicine," 1912, vol. v.)

The Nature of the Condition termed Parasyphilis.

By F. W. MOTT, M.D., F.R.S., F.R.C.P.

Report to the Neurological Section of the International Medical Congress held in London, August, 1913.

The report was sent in February, 1913, to the Secretary ; since then, owing to the discovery of the spirochaete in the brains of general paralytics by Noguchi, the views regarding tabes and general paralysis being of a post-syphilitic nature have been given up, and it has become necessary to modify my original report considerably, although in that report I advanced many reasons for supposing that the organism was still present in the body in a latent form, possibly as an infective granule or intracellular organism.

SUMMARY.

1. Introduction. Parasyphilis (or metasymphilis of German authors) applied by Fournier to a number of diseases of the nervous system arising in subjects of acquired or congenital syphilis. Especially tabes and general paralysis considered.

2. Erb's spastic paraplegia. Reasons for supposing it to be syphilitic focal meningo-myelitis.

3. Parasyphilis characterised by mild forms of syphilitic infection. Hypothesis relating to the cause of this mild form of infection in tabes and general paralysis. Latent syphilis, a common condition. Its relation to immunity or partial immunity. The modification of the specific organism. The influence of widespread mercurial treatment. The syphilitic organism latent in the nervous system. A specific spirochaete with a neurotoxic action. Evidence thereon.

4. Relation of the Wassermann reaction to parasyphilis of the nervous system and syphilis of the nervous system. The cerebro-spinal fluid. The relation of complement fixative in fluid obtained from ventricles and by lumbar puncture to pathology of general paralysis of the insane.

5. Contributory factors in the production of tabes and general paralysis. The neuropathic inheritance in relation to general paralysis. Statistics of general paralysis in 3,118 relatives admitted to the London County Asylums. No indication of a close relationship of heredity as in the truer insanities.

2 *The Nature of the Condition termed Parasyphilis.*

6. Congenital syphilis and general paralysis.

7. Comparison of East London and West London population. Greater incidence of male paralytics in West-end parishes. Slightly greater incidence of female paralytics in East-end parishes.

8. The discovery of the spirochaete in the brain in general paralysis. Noguchi and Moore. Confirmation by others, including personal observations. The existence of the parasites in the parenchyma of the nervous system in relation to their resistance to the action of drugs.

9. Recent developments in the treatment of general paralysis and tabes.

The term parasyphilis was introduced by Fournier, to whom especially we owe the recognition of parasyphilitic disease of the nervous system. The following list of affections were according to him parasyphilitic manifestations of acquired syphilis :—

- 1.—(1) Acute hystero-neurasthenia of the secondary stage.
- (2) Various neurasthenic manifestations of a more advanced stage.
- (3) Hystero-syphilis.
- (4) Tabes.
- (5) General paralysis.
- (6) A special form of muscular atrophy.

II.—Heredito-syphilis (more correctly speaking congenital). Numerous dystrophic troubles (general or partial), malformation (notably dental), arrest or retardation of physical and intellectual development, infantilism, dwarfism, inborn lack of vitality, cachexia, marasmus, rickets, hydrocephalus, certain forms of simple meningitis in early life, possibly certain cases of true epilepsy, juvenile tabes and juvenile general paralysis.

This is not the whole list, but it is sufficient to show that as long ago as 1894 Fournier regarded parasyphilis as a much wider entity than did most neurologists and syphilidologists ; in other words, he included many nervous diseases besides those which are universally reckoned as parasyphilitic. These are tabes dorsalis, optic tabes, tabo-paralysis, and general paralysis ; in fact, nervous diseases in which characteristic pupil phenomena are invariably met with at some stage of the disease and in case of the Argyll-Robertson sign not met with in any other disease (except in a few cases of tumour of the third ventricle), not even in syphilitic brain disease.

There is some evidence that some cases of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy may be included under the same pathological group of parasyphilis. It is assumed that these conditions when occurring in combination with tabes or general paralysis are due to the same pathological process, and therefore when occurring uncombined are of the nature of parasyphilis. Dr. Wilson in a recent review of the subject

affirms that :—" If the question of antecedent syphilis were carefully investigated in every case of primary optic atrophy, primary lateral sclerosis and progressive muscular atrophy, or better still if every case were subjected to the Wassermann test as well, I believe that an accumulation of evidence entirely analogous to that obtained in the etiology of tabes and general paralysis would soon be at hand, and that these three diseases wandering in the wilderness of undiscovered causes, would take their place amongst the rarer manifestations of parasymphilis of the nervous system."

In respect to lateral sclerosis in conjunction with tabes and primary lateral sclerosis, Erb's spastic paraplegia, I have recently had under my care a case exhibiting tabetic pupil phenomena ; small, irregular in outline, inactive to light, active to accommodation with well-marked signs of lateral sclerosis.

J. McC., aet 46, tailor ; syphilis at 29. At the age of 44 he began to lose power in his legs and suffered with bladder trouble ; he was sent to me as an unusual case of tabes. He had weakness and wasting of the legs and foot drop, loss of control of the bladder necessitating evacuation by catheter ; he had pus in the urine from cystitis which, however, cleared up with treatment ; no feeling of tightness around the chest, and no thoracic or abdominal anaesthesia. There was exaggeration of all the deep reflexes with a well-marked planter extensor response. There were only very slight sensory disturbances in the nature of delay and blunting of sensations in the lower extremities. The abdominal reflex was absent. The Wassermann reaction gave a well-marked positive reaction ; this disappeared after 30 injections, and he improved greatly with massage and exercise in the open air, so that he can now get about with the aid of a stick. The question arises why have not the symptoms and signs of lateral sclerosis in this case originated in the same pathological process as that which caused the tabic phenomena ? If there had been no Argyll-Robertson pupil this might have passed for a case of either Erb's spastic paraplegia or of focal meningo-myelitis.

Erb, in 1892, described a group of cases occurring in the subjects of syphilis which he considered distinct from focal meningo-myelitis in the dorsal region and due to a primary degeneration in the ascending cerebellar and posterior median tracts and the crossed pyramidal tracts. The symptoms of the primary sclerosis occur later, and there develops gradually a spastic paresis of the legs with marked increased deep reflexes ; although the gait is extremely spastic the muscular contraction is but slight. The bladder is early and almost constantly affected. Disturbances of sensibility are usually present, but only slightly manifest. The course is chronic in most cases and there is a tendency to improvement, to remissions, and even to complete arrest.

Numerous neurologists, including Oppenheim and Marie, asserted that

these cases were really due to a syphilitic meningo-myelitis. Since that time nine or ten cases of typical syphilitic spinal paralysis with post-mortem examinations have been published. These cases are those of Westphal, Eberle, Max Nonne (two cases), Williamson, Long and Wiki, Dreschfeld, Wimmer and Renner.

Max Nonne concludes that although syphilitic spinal paralysis is clinically a well-defined entity, it has by no means a constant unvarying morbid anatomy. Two cases which have come under my observation and have died showed an annular sclerosis due to an old meningo-myelitis; in neither case, however, was there, as in the case narrated, the typical tabetic pupil phenomena.

Muscular atrophies occasionally occur in tabes and more probably than earlier writers allowed. Cases have been described by Dejerine, Souques, Marie, Odds, Camp, Kinnier Wilson and Rayner, and I have myself described a case of amyotrophic tabes with microscopical investigation of the anatomical changes in the nervous system. Marie and Leri believe that spinal amyotrophic lateral sclerosis may in many instances be due to the action of the syphilitic poison. They base this conclusion upon the frequent history of syphilis in patients suffering with this disease, and upon the fact that a number of cases have been recorded where although syphilitic infection was not certainly proved yet concomitant affections such as tabes dorsalis and general paresis were observed; this accords with my own experience.

Although I think it can be admitted that a primary degeneration of, or arrest of development of any neuronie systems may occur as the result of a past syphilitic affection, nevertheless, the fact remains that those nervous diseases in which the characteristic pupil phenomena occur, are especially the affections which will be discussed as regards their relationship to syphilis. Still, the pathology of the diseases in question, may be easier to comprehend, if it be admitted that antecedent syphilis can occasion in some instances degenerative processes in some portion or even the whole of the motor efferent path from cortex to muscle.

The parasyphilitic affections which will be discussed as regards their relationship to syphilis are:—

- (a) Tabes dorsalis.
- (b) Tabes optica.
- (c) Tabo-paralysis.
- (d) Paralytic dementia.

All these degenerative conditions of the nervous system are now recognised by neurologists and psychiatrists to be due to the action of the virus of the specific organism of syphilis, the *spirochaeta pallida* in the central nervous system. The patients are still immune to re-infection as experiments and

observations have clearly demonstrated. Again, cases of syphilitic skin lesions in patients suffering with general paralysis and tabes have been reported in which the skin lesions have been cured by anti-syphilitic remedies, but the nervous affection was neither arrested nor cured. As a rule its anti-syphilitic treatment has had comparatively little beneficial effect; especially is this the case in general paralysis, where the pathological process is most active in the form of a meningo-encephalitis; whereas in a gummatous meningo-encephalitis active treatment with salvarsan or mercury acts like magic. The inefficacy of treatment was one of the main arguments used against parasyphilitic affections being of the nature of a "quaternary syphilis" as Bosc, Hirschl, Lesser and Nageotte asserted before the discovery of the spirochaete in the brains of paralytic demented by Noguchi, which confirms the views of the above-mentioned authorities. Bosc affirmed with correctness, that there is a general similarity in the lesions of general paralysis and tabes to other syphilitic lesions, viz., there is an endothelial and connective tissue (neuroglia) hyperplasia with a tendency to fibrous and sclerous formation. But in tabes and especially general paralysis there is more than this; there is a primary neuronie decay which we cannot account for solely by the chronic inflammatory changes observed in the supporting, enclosing and nutrient tissues, the same as we can in coarse syphilitic lesions, *e.g.*, gummatous meningitis, peri-arteritis and endarteritis, which commonly occur within the first few years after infection.

PARASYPHILIS CHARACTERISED BY MILD FORMS OF SYPHILITIC INFECTION.

Fournier and practically all those who have followed him in recognising syphilis as the cause of tabes and general paralysis, have been struck by the fact that the cases which subsequently developed these diseases were more often than not characterised by indefinite or very mild signs of primary infection, secondary symptoms and tertiary manifestations.

This has certainly been my clinical experience in hospital and asylum practice. Moreover, I have been particularly struck by the fact that I do not remember having seen during life or after death on the post-mortem table, a primary sore or secondary eruption, although my opportunities have been very great during the last 16 years that I have been pathologist to the London County Asylums with a population now numbering 20,000. I have notes of 600 general paralytic autopsies made at Claybury Asylum, and I have observed that the external marks of syphilis in the form of skin visceral and bone lesions in these cases are slight and relatively few in number. Enlargement of lymphatic glands, gummata, or scars of gummata of the skin and well-marked papery scars have been comparatively rarely met with. When they have

occurred in a well-marked form, the case which during life was diagnosed as general paralysis has generally turned out post-mortem to be one of pseudo-general paralysis, a syphilitic brain disease with widespread coarse lesions, *e.g.*, multiple gummata, endarteritis, peri-arteritis and generalised gummatus meningitis. I may remark that these cases of pseudo-general paralysis have been seen by me far less often than formerly in my asylum practice. I believe that this is due to a wider knowledge among medical men of the incidence of syphilis of the nervous system in the first few years after infection, consequently the earlier diagnosis and better treatment of cerebral syphilis of recent years.

Gummata or scars of gummata of the viscera are very rare in general paralysis; in fact, the only evidence of antecedent syphilis found internally in general paralysis in a considerable number of cases is nodular fibrosis of the aorta, and this is present in some degree in rather more than one half of the cases (see page 54). It is unusual to find any evidence of obvious cerebral endarteritis in general paralysis.

In a not inconsiderable proportion, 20 to 30 per cent., of cases of general paralysis there may be no history and no signs on the body of antecedent syphilis; yet, as we shall see later, practically all cases of general paralysis give a positive Wassermann reaction of the blood and cerebro-spinal fluid, usually in all dilutions. This fact, coupled with the experimental inoculation of nine general paralytics who showed no sign of antecedent syphilis and gave no history of infection, with negative results, related by Krafft-Ebing, proves fairly conclusively that syphilis is an essential factor in the production of this disease. Consequently, in any attempt to solve the relationship of syphilis to parasyphilitic affections, one question of importance requiring an answer is this: Why do people suffering with general paralysis and tabes as a rule suffer with such mild or indefinite signs and symptoms of infection?

HYPOTHESES RELATING TO THE CAUSE OF THIS MILD FORM OF INFECTION IN TABES AND GENERAL PARALYSIS.

(a) They have a natural or acquired immunity or partial immunity, owing to widespread racial syphilisation having eliminated in time all those who would have the disease in a virulent form, or they possess an immunity due to parental syphilis.

(b) The specific organism that has caused the infection has become modified by passage through individuals who are partially immune or who have been treated with mercury.

(c) There may be several forms of spirochaetes as there are several forms of trypanosomes, and as in the case of *trypanosoma gambiense*, one form of

spirochaete may have acquired a habit of entering the cerebro-spinal fluid and central nervous system as a safe retreat.

IMMUNITY OR PARTIAL IMMUNITY.

Syphilitic infection is followed by very different results in different individuals. Is this due to the virus or the resistance of the individual? Thus I had a case of juvenile general paralysis who was the son of a respectable professional man, who acquired syphilis; he was treated with mercury for three years and did not marry till five years after infection. His wife had five conceptions; the first two died within two days of birth; the third lived but suffered with syphilis tarda in the form of keratitis and nerve deafness; the fourth developed general paralysis at 13 and died at 15 years of age; the fifth is alive and well. The mother must have been syphilised although she did not suffer in any way.

As a contrast to this case, I may mention the following:—R. D., a carpet planner, who suffered with tabes, gave the following history of conceptions following his marriage at 22, which was just two years after he had contracted syphilis with a hard chancre, for which he was treated with mercury for only two months. The first child was born within one year of marriage and is alive and well; he has had six healthy living children, one of whom died aged nine; there were also twins born prematurely at six months.

We may explain the different results on the offspring in the two cases by the infection of the wife of the former, although the man was treated for years with mercury, and the non-infection of the wife of the latter, although the husband was inadequately treated. It is a rational conclusion to arrive at, that the former possessed far less natural resistive powers to the action of the virus than the latter who developed subsequently tabes dorsalis.

I could multiply instances of this kind, to show that the virus must vary, or the defensive reaction of the individual must vary considerably in different persons. Of course it might be asserted that in the former case the spirochaete had infected the testis and the semen in consequence was infective, whereas in the latter case the testis had not been involved. On the other hand, seeing that it is a rule for parasyphilitic cases to suffer with very mild and indefinite symptoms, so that they are very often not treated, it is more likely that the non-infection of the wife in the latter case was due to a natural increased defensive reaction of the tissues and fluids of his body. It might, however, be explained by his having been infected by a modified specific organism.

Recent researches by the Wassermann reaction of Plaut, Boas and others, which I can confirm by my own experience,* show that a large number of

* I am indebted to Dr. Topley, Clinical Pathologist to Charing Cross Hospital, and my assistants, Dr. Candler and Mr. S. Mann, for the results of the Wassermann reaction.

children and young adults apparently in good health born of syphilitic parents are the subjects of latent syphilis and are therefore immune ; some of these in later life and without treatment lose this immunity. We know obvious congenital syphilitics with stigmata are only rarely reinfected ; so it is more than likely that children apparently healthy, born of syphilitic parents, may have either a partial or complete immunity to the acquirement of the disease in later life. Neisser states that successful re-inoculations are very rare in animals, but when they occur they run a course without glandular swelling and the especial phenomena which accompany the true syphilitic chancre. It is, however, probable the longer he kept his animals alive after the primary infection, the greater would be the number of successful re-inoculations followed by these indefinite phenomena.

According to Neisser if there be a complete immunity the spirochaeta pallida is still present in some form or other in the body. In support of this hypothesis, I may mention that Neisser in his experimental investigation on apes, has observed that the tissues of infected animals in which no spirochaetes were demonstrable could nevertheless be used successfully for inoculation.

From observations on trypanosome diseases of the nervous system I thought it probable that there might be a granule intracellular form of the syphilitic spirochaete which remains latent and subsequently develops into the spiral form. The observations of O'Farrel and A. Balfour show that the injection of salvarsan has the effect of causing a shedding of granules, but that this occurs also independently of the action of any drug. This phenomenon is not confined to the specific spirochaete of syphilis, it occurs in other forms met with in the primary sores. Salvarsan increases the granule discharge, and these authorities consider that the discharge is protective, undertaken by them with a view to prevent their total extinction, the granules being of the nature of resistance spores, the further history of which remains unknown ; but which, so far as those derived from spirochaeta pallida are concerned, doubtless play an important part in relapses and in the later manifestations of syphilitic infections. Noguchi has observed that in pure cultures of spirochaeta pallida under certain conditions, enormous numbers of minute granules occur, and that from these granules after transference to a passive culture media spiral forms again sprout out. E. H. Ross and McDonagh have described intracellular forms and a complete cycle of development.

The important researches of Leishmann on the spirochaete of tick fever, showing that in this disease there is an intracellular phase of the spiral organism in the form of chromidian granules, supports the hypothesis of a latent resistive granule intracellular form. Chromidian granules are contained in the spirochaeta pallida and may be seen often in enormous numbers where

the spirochaetes are found. Spengler claims to have discovered an ovoid bacillus which inoculated into rabbits produces a gummatous-like tumour containing spirochaetes in pure culture. By retro-inoculation a pure cultivation of granules grew which again merged into ovoid short rods of the first culture. There are reasons therefore for supposing that a granule phase of the organism may form latent foci of infection giving rise to these late manifestations of syphilis.

There is evidence to show that immunity in all protozoal diseases is due to the existence of the parasite in the body ; it may be harmless to the host, but it is there. Its harmlessness may, however, be due to the continuous production of some defensive reaction of the body which prevents its generalisation in the fluids and tissues of the body, or which inhibits the life cycle of the organism, or modifies it biologically.

LATENT SYPHILIS : A COMMON CONDITION ; ITS RELATION TO IMMUNITY.

In my studies of 60 cases of general paralysis of the juvenile form, the history obtained from the mothers concerning conceptions was similar in most cases, viz., miscarriages, still-births, children dying in infancy of convulsions, meningitis, and of hydrocephalus, followed by children who lived and who later developed syphilis, hereditaria tarda, primary optic atrophy, and other so-called parasymphilitic diseases, *e.g.*, juvenile tabes and juvenile general paralysis.

In 20 per cent. of these cases one of the parents, usually the father, had died of general paralysis. In these researches I have been struck by the number of mothers of such patients, who have said, they have never ailed and in whom one could find no obvious signs of syphilis, nor by questioning them, could I obtain any history of symptoms ; although the history of pregnancies clearly pointed to their having been infected. I have recently had the opportunity of examining the bloods and cerebro-spinal fluids of two of these cases of juvenile general paralysis ; both gave a positive reaction in the blood and the cerebro-spinal fluid. The bloods of the mothers of these two patients were both positive, although they have never suffered in any way and were quite unconscious of the fact that they had been infected. They were, like all cases of mothers of syphilitic children who have not suffered from any symptoms, cases of latent syphilis, and in the majority of cases these mothers have received no specific treatment. Yet Neisser's researches indicate that the organism must still be present in the body. To what then do they owe this immunity to harmful results and absence of symptoms while their offspring suffer ? Spirillocidal substances must be manufactured in the body of the mother in sufficient amount to destroy the organism in the maternal system, but not enough to destroy them in the foetus. Probably the foetal tissues

form a better soil for the syphilitic organism to grow in ; a rapid multiplication occurs in the tissues of the foetus which may lead to a great amount of bio-chemical sensitising substances being formed in the circulating blood of the foetus. The placental villi may permit this to pass into the maternal circulation but not the specific organisms ; the result is a stimulating effect upon the cells of the maternal tissues with the production of increasing amounts of spirilloidal substances sufficient to protect the mothers in the first pregnancies, but not enough to protect the foetuses of the earlier conceptions, owing to the active development of the organisms out of proportion to the defensive reactions of the maternal blood. The defensive reaction of the mother must, however, increase with each successive pregnancy until a living child is born. Now there must be a great number of instances of latent syphilis in mothers of even apparently healthy children, and the interesting question which naturally arises is, whether these children, born of mothers with latent syphilis, if infected in later life, suffer with a mild form of the disease, such as so frequently occurs in tabes and general paralysis.

Plaut has shown by sero-diagnosis, that congenital syphilis is much more common than was formerly supposed, when reliance was placed solely upon the history, signs, or symptoms of congenital syphilis. The observations of Plaut and Göring show that one-third of the living children of paralytics give the reaction. An interval of eight years after infection may occur and the children born within that period may show the reaction, but the shorter the interval between infection and the birth of the child, the more marked is the reaction and the more likely is it to occur. Every woman that brings into the world a syphilitic or a parasyphilitic child is herself syphilitic and immune, and a number of her living offspring are also immune or partially immune. We have, therefore, with widespread racial syphilisation to admit the probability of a great number of latent congenital syphilitic beings and individuals possessing a partial or complete immunity by an acquired defensive reaction on the part of the tissues of the body.

The researches of Plaut are of interest and important in this connection ; he examined 54 families of paralytics and found 31·6 per cent. of the wives of paralytics were positive ; 37·5 per cent. of the husbands of paralytic women were positive, and in only 38 per cent. was a transmission of the syphilitic infection to a spouse or offspring not found. The cases with a history of syphilis and clinical evidence of transmission of syphilis were remarkably few. Of the 26 certain and 8 probable infected children, not one was treated with anti-syphilitic remedies, and in only one was a syphilitic rash diagnosed, and this did not receive any treatment ; in all the remainder not one had been thought to be suffering from congenital syphilis. In the wives of paralytics

it was scarcely better ; in no case had mercury been administered, and only one woman had received potassium iodide for a syphilitic periostitis.

Accepting the premise that a positive Wassermann reaction in children even without any obvious signs of the disease is to be regarded as "latent congenital syphilis," and that owing to widespread racial syphilisation, latent congenital syphilitics are far more numerous than is generally suspected, it is conceivable that there exists a great number of individuals so affected, who are either incapable of superinfection, or if later in life they acquire the disease, suffer in the mild form which Neisser has shown occurs in animals that suffer with a second attack after re-inoculation. The liability of persons suffering with tabes and general paralysis being individuals born of syphilitic parents seem possible, when it is remembered that only 3 to 5 per cent. of cases of syphilis develop these late forms of disease of the nervous system, tabes and dementia paralytica. Moreover, facts seem to show that McIntosh and Fildes are justified in stating that a large degree of insusceptibility to superinfection occurs in congenital syphilitics ; in the milder cases of infection, however, the immunity may only be partial, while after a lapse of years the defensive reaction may subside and with it the resistance to superinfection ; this would agree with clinical experience and the fact already pointed out that syphilitics who develop these late manifestations (quaternary) have nearly always suffered with a very mild form of primary and secondary symptoms.

The idea of such an immunity is supported by the fact that it is conceivable that a foetus in utero may be partially immunised by the passage of dissolved substances through the placenta from the mother, and this passive immunity may account for the freedom of symptoms commonly shown by infants during the first few months of life. The discovery of Boas that healthy infants of syphilitic women may show at birth a transient Wassermann reaction may indicate the passage of anti-bodies through the placenta. I recently had my attention called by Dr. Clarke of Banstead Asylum to a female paralytic who was pregnant. She gave birth to a healthy full-term child ; we found that both the mother's blood and that of the infant gave a positive reaction. The cerebro-spinal fluid of the mother gave a positive reaction, also excess of lymphocytes. It is possible that if the Wassermann complement-fixing substance is capable of crossing the placenta to the child, protective substances may also do so. This child was tested again two months later, it still gave a positive reaction but was quite healthy although it had had no treatment. This incident suggested to me the useful results which might be obtained by a systematic examination of the blood of a large number of children at birth ; the blood being procured when the umbilical cord is divided.

Neisser in his magnificent monograph "*Beiträge zur Pathologie und*

Therapie der Syphilis," when discussing the existence of anti-bodies, refers to the work of Taege, Duhot, Dobrovitz and Raubischek, who have shown that by treatment of a syphilitic mother with arseno-benzol, anti-bodies existed in the serum which were conveyed to the suckling infant by the milk, and led to the removal of the visible symptoms and the cachexia in the infant. Meyrowski and Hartmann, also Scholtz, were able to influence favourably the symptoms of congenital syphilis by subcutaneous injection of serum of persons treated with 606. The amount of arsenic present was not sufficient to account for the effect produced. It is assumed that curative spirolytic substances are produced by the arseno-benzol treatment. Whether immunity bodies are produced is still unproven. McIntosh and Fildes state, "the possibility of the presence of anti-bodies in syphilis has been brushed aside too lightly. Even if there were no evidence of their presence this could not be taken as evidence against their presence. When cultures or their substitutes are obtained there is no reason to suppose that specific anti-bodies will not be found in syphilis as in the other spirochaetes." The principle of the presence of anti-bodies in the serum of patients treated by salvarsan has been applied therapeutically. (See pages 44-48.)

The question then arises whether in tabes and general paralysis there may not be an acquired or inherited hyper-sensibility of the cells of the body generally to react to the virus by the production of anti-bodies. The relative infrequency of tabes and general paralysis in a race recently syphilised, where this acquired immunity has not had time to take place, supports this argument. The interesting description given by Colonel Lambkin of the syphilisation of the natives of Uganda shows how severely a race previously free from this disease suffers from malignant skin, bone and visceral disease. He also points out that the so-called parasyphilitic affections are rare, the reason being that the disease has not existed in the country a sufficiently long time to allow of their frequent occurrence. This accords with Von Duhring's observations in Asia Minor. Von Halban has stated that tabes is as common in Abyssinia as in Vienna, but syphilis has long been existent in that country. Sir Charles Lukis, the Director General of the Indian Army, has informed me that although syphilis is extremely common in India, yet general paralysis is rarely met with.

In the discussion of the Wassermann reaction in relation to the question of syphilis and parenchymatous syphilis (the so-called parasyphilis), a number of facts will be stated, tending to show that normally the existence of the syphilitic organism in the body, whether active or latent, does not excite a Wassermann reaction in the cerebro-spinal fluid unless there is evidence of syphilis of the nervous system, and by no means always then unless there be signs of paralytic dementia.

THE MODIFICATION OF THE SPECIFIC ORGANISM.

The specific organism may have become modified in its form and habits, so that there is a tendency for it to become latent in the tissues; possibly, as previously suggested, it may take on an intracellular granular form. In support of this argument I may mention that Neisser was able to infect monkeys with the bone marrow of infected animals; although the most diligent search failed to find spirochaetes in the material used for inoculation. As in most protozoal diseases the organism may disappear from the blood under the influence of treatment or by the action of the natural defences of the body. Should the natural defences be weakened by any cause, *e.g.*, traumatic injury, or disease, alcoholism, &c., the organism may become active.

Neisser suggests that the widespread use of mercury in the treatment of syphilis may have modified the specific organism. By analogy it is conceivable that there are "mercury fast" spirochaetes as the experiments of Ehrlich show that there are "arsenic fast" trypanosomes. This hypothesis is compatible with two facts: (1) that the average time between infection and the development of tabes or general paralysis is 10 years, and it is the same whether the patient has been treated with mercury or not; (2) neither of these diseases are benefitted to any great extent by mercurial treatment, and general paralysis up to the present, not by any anti-syphilitic treatment. Upon this hypothesis it may happen that a person who has been taking mercury for some time has eliminated all the spirochaetes except the "mercury fast"; this individual communicates the disease to another who is thus infected with "mercury fast" organisms.

THE INFLUENCE IN THE PAST OF MERCURIAL TREATMENT IN THE MODIFICATION OF THE VIRULENCE OF THE SPECIFIC ORGANISM.

We do not, however, know whether mercurial treatment may not have led to the spirochaete taking on a latent form and hiding away in tissues where mercury does not readily penetrate. We know that mercury taken into the body in any form or by any method comes out by the skin, and with the widespread use of mercury the spirochaete may have been modified; it is conceivable that by acquiring a new habit of remaining in some internal tissues which mercury does not affect to the same degree as the skin, the specific organism of syphilis acquires a new habit.

That these protozoa do take on new habits of preservation is shown in the case of the trypanosoma equiperdum which produces the *mal de coit* of equines; this trypanosome is not carried by a fly, but by its multiplication in the secretions of the mucous orifices, it is transmitted from one animal to another by

coitus ; and a fly or biting insect as an intermediate host, is unnecessary. It is remarkable that in this disease, the animals, if they survive several years, suffer with ataxy and lesions of the posterior spinal ganglia, posterior roots, and posterior columns like those of tabes. It may be assumed that the lesion is the result of a toxin produced in lymphatic structures of the internal organs which are directly or indirectly connected with the perivascular and neural lymphatics that enter the posterior columns of the cord along the posterior roots. I have described the lesions in five cases sent to me from India by Dr. Lingard. Spielmeyer has inoculated animals with trypanosoma equiperdum, and produced lesions of the posterior columns resembling tabes. The interesting and carefully devised experiments of Orr and Rows show that toxins enter in this way the posterior columns of the spinal cord and produce plasma cell and lymphocyte perivascular infiltration associated with degeneration of the intra-spinal portions of the afferent exogenous systems. In tabes, however, there is no clear proof of the existence of latent syphilitic foci in the internal structures capable of emitting a continuous stream of toxin into the lymphatics connected only with the posterior columns, unless it be by toxins arising from lesions of the aorta caused by spirochaete metastases, the evidence of the existence of which is forthcoming in the nodular fibrosis so commonly met with in tabes and general paralysis ; consequently it is possible that the perivascular lymphatics of the blood vessels and nerves entering the cerebro-spinal axis may convey toxins, infective granules or spirochaetes from these and other unknown internal lesions to the cerebro-spinal axis, setting up as Pierre Marie and Guillain long ago suggested a syphilosis of the posterior lymphatic system of the spinal cord and thus giving origin to the anatomopathological process of tabes. The infection of the brain by spirochaetes may arise by perivascular lymphatics proceeding from lesions of the aorta along the carotid arteries, and this may account for the fronto-central regions of the brain being especially the seat of the degenerative process. If this is the case it is remarkable that one does not find more evidence of lymphatic gland enlargement in these parasyphilitic infections. In sleeping-sickness a striking feature is the polyadenitis ; moreover, puncture of the glands is a ready mode of finding the trypanosomes.

THE SYPHILITIC ORGANISM LATENT IN THE NERVOUS SYSTEM.

At the "Congress fur Innere Medicin zu Wien," 1908, s. 202, Salamon emphasised the rarity of the combination of skin and bone diseases with simultaneous tabes and paralysis, and he made the following pronouncement :—
 "I would prefer every syphilitic person should exhibit a skin syphilide within

two or three years of infection, then should I be assured that he will neither suffer with tabes or paralysis"; at least this accorded with his experience he said, and there have been but few exceptions. He, moreover, stated that he wished he could make all latent syphilitic subjects artificially exhibit skin eruptions; for we should perhaps be able thereby to preserve them from the dangers of metasymphilis.

Kraus and Neisser, in the discussion that followed, said that immunity of the skin does not imply that the internal organs are unaffected, and the latter affirmed that his experiments in no way point to an opposition of skin immunity to organ immunity, nor does his clinical experience support this view.

Finger took part in the discussion raised by Salamon and expressed the view that on the whole an opposition does exist; on the one hand favourable progressive syphilis is associated with abundant and intense skin eruptions, and on the other hand the more dangerous cases in which skin lesions are slight are more often associated with involvement of the internal organs.

Neisser admits that these facts may be right; certainly a cutaneous syphilide is less harmful than a visceral or parasymphilitic affection, but the observation of Salamon that the visceral organs and the nervous system are less affected because the skin is more markedly affected is not supported by any evidence.

Lang long ago pointed out that slight meningeal symptoms may arise before the primary sore is healed and during the roseolar rash. I have myself observed such cases; it was ridiculed by no less an authority than Gowers, but in the light of recent research it is obvious that spirochaetal metastases may occur in the membranes of the central nervous system as they occur in the skin causing an eruption; and recently Sezary has again called attention to the fact that there may be a very early form of meningitis due to infection, only discoverable by lumbar puncture disclosing a lymphocytosis. It is in the first stage that one must intervene with treatment to prevent subsequent development of parasymphilis, says this authority. But we know that there are an immense number of cases which have been treated systematically with mercury from the very first and yet in later years have developed tabes or general paralysis. The hope of prevention of infection of the nervous system lies in the prompt diagnosis of the nature of the primary infection by examination of the exudation from the primary sore for the specific spirochaetes. If necessary the research should be made several times in the case of every venereal sore; for it is the supposed soft sore with mild secondary symptoms which is so dangerous. As soon as the syphilitic nature of the sore is discovered, intravenous injection of salvarsan should be employed; followed up by prolonged courses of mercury. Seeing that since this treatment has been adopted numbers of cases of re-infection have been reported, it may be

presumed that the organism has been destroyed ; consequently it may be inferred that such treatment may in numbers of cases prevent a generalisation in the blood and lymph streams and infection of the internal organs, including the nervous system and aorta, when the roseolar rash or secondary symptoms occur.

Neisser's experiments on animals show that immunity to re-infection depends upon the existence of the specific organism in some form or other in the body. He bases this conclusion upon the following facts : (1) almost all animals incapable of re-inoculation were still ill ; (2) animals, which by curative methods had been freed from disease, were correspondingly capable of being infected ; (3) he knows no reason why the analogy should not be applied to man.

The negative results of syphilitic inoculation of general paralysis, according to Finger, prove nothing more nor less than that such individuals are immune to re-infection ; never, however, that they are not syphilitic. Neisser affirmed that the spirochaete pallidum existed in the body in tabes and general paralysis because the subjects of these diseases are incapable of re-infection. He moreover states : " Really one would think that in respect to these diseases, the degenerations are already present in the very early stages of syphilis, even though the clinical phenomena do not occur till later." Recent researches (see pages 34-42) show that Neisser was right in the assumption, for we shall probably come to the conclusion that the spirochaete exists in the brain in every case of general paresis.

Those authorities who consider the lesions of tabes and paralysis to be due to the direct exciting action of the specific organism upon the neurones and the mœsoblastic structures, and in favour of this cite the fact that the perivascular lymphocyte and plasma cell infiltration with glia cell proliferation are similar in sleeping-sickness, general paralysis and syphilitic brain disease, are confronted by the difficulty of explaining the elective action of the poison in the production of degenerative changes, viz., how does this theory explain the Argyll-Robertson pupil, and the affection of the intra-medullary portions of the afferent spinal proto-neurones in tabes, the motor being entirely spared ? In gummatous cerebro-spinal meningitis, which is due to a generalised infection of the lymphatics by the specific organism, there is no elective degeneration. Random generalised lesions occur giving rise to random coarse obtrusive symptoms. The elective affection of the posterior spinal protoneurones may, however, be explained by the passage of a toxic or exciting agent entering the cerebro-spinal axis by the lymphatics of the vessels and nerves continuous with the structures in the posterior roots.

I shall later adduce evidence in favour of the view that in dementia

paralytica a toxin is produced by the active multiplication of the spirochaetes in the brain, which escaping into the cerebro-spinal fluid irrigating the brain tissues, excites the neurones of the cortex in the neighbourhood of its production, and by its action combined with contributory causes connected with circulatory disturbances and congestive inflammatory stasis, leads to neuronie decay. The epileptiform seizures, the transitory hemiplegias, aphasias, and paraphasias are but the clinical manifestations of the production of the toxin by a latent form of spirochaetes becoming active and multiplying.

A SPECIFIC SPIROCHAETE WITH A NEUROTOXIC ACTION.

There may be different varieties of spirochaetes of syphilis as there are different varieties of trypanosomes, the morphological character of which would not permit of differentiation. It is not impossible that a spirochaete may exist which has an affinity for taking up its habitation in the central nervous system, as we know that the trypanosoma gambiense has; or there may be a specific organism endowed with a particular toxic action on the nervous system. Whatever there be, etiological facts are sufficiently numerous now to show that certain individuals who are a source of infection to others are able to transmit a virus that is especially liable to cause general paralysis or tabes in the persons infected by them. The following examples may be cited in support of this theory. I have recently heard of two doctors, not related, who acquired syphilis from the same nurse; 10 years later they developed general paralysis. Marie and Bernhard relate the instance of two men who were infected from the same source and 10 years later suffered with tabes. Erb narrates an instance of four patients infected by the same woman, who later became the subjects of either tabes or general paralysis, whilst a fifth who had connection with the woman, but was not infected, did not suffer from any disease later. Morell Lavallée has given the following striking example:—

Martha X.				
May, 1870.	December, 1871.	January, 1872.	Later.	Still later.
Mistress of <i>Primus</i> (medical student) and gave him syphilis. He died 1873 of syphilitic meningitis.	Mistress of <i>Secundus</i> (medical student), to whom she gave syphilis. He married later, had two healthy children, and died 1888 of general paralysis.	Lived four years with <i>Terminus</i> (medical student). He married later, had two healthy children, and died 1882 of general paralysis.	Mistress of <i>Quartus</i> (chemist). He died 1890 of general paralysis.	Mistress of <i>Quintus</i> (engineer). He died (no date) of syphilitic insanity.

These cases may have been the result of coincidence, but they make us reflect on the possibility of a specific neuropathic organism. Probably the most striking example supporting this theory of a specific organism attacking the nervous system is that recorded by Brosius, who related that seven glass-blowers suffered with chancre of the lip, and out of five, who 10 years later came under observation, four suffered with either tabes or general paralysis.

COMPARISON OF THE MORPHOLOGICAL CHANGES IN SLEEPING-SICKNESS AND GENERAL PARALYSIS.

Accepting the fact that the invasion of the body by the *spirochaeta pallida* is the essential direct or indirect causal agent in the production of tabes and dementia paralytica, it is quite conceivable that there may be varieties of the organism as there are of the malarial parasite or trypanosome. In sleeping-sickness there is an invasion of the cerebro-spinal fluid by the *trypanosoma gambiense*, and there is reason to believe that when this occurs, the disease leads to a characteristic chronic meningo-encephalo-myelitis, causing a progressively increasing lethargy which invariably and in spite of treatment, eventually proves fatal. However, the trypanosome can in all cases be recovered from the fluid by lumbar puncture, and we must believe that it is the invasion of the cerebro-spinal fluid by the organism which is the essential cause of the chronic inflammatory lymphangitis of the cerebro-spinal axis. Seeing that no therapeutic agents such as arsenic, antimony or mercury can enter the cerebro-spinal fluid from the blood stream, the parasite finds a safe retreat here and it serves as a constant source of re-infection of the blood stream. The *spirochaeta pallida* has been very seldom if ever demonstrated in the cerebro-spinal fluid of syphilis of the nervous system. Dohio and Tanaka claim to have observed spirochaetes in the fluid.

Nicholls and Hough have claimed to have demonstrated the existence of *spirochaeta pallida* in the cerebro-spinal fluid from a patient with nervous relapse following upon the use of salvarsan ("Journ. Amer. Med. Assoc., 1913, lx, 108. See also my own experience, page 46). Hoffmann certainly succeeded in infecting a monkey with blood free cerebro-spinal fluid withdrawn by lumbar puncture from a person suffering with syphilitic meningitis.

The meningeal lymphatic and perivascular lymphatic changes with infiltration of lymphocytes and plasma cells and neuroglia proliferation in sleeping-sickness closely correspond with the changes met with in general paralysis of the insane; the essential difference in the histology of the two diseases, however, is this: that whereas there is in general paralysis an atrophy of the cortex cerebri proportional to the duration of the disease and the degree

of dementia, in sleeping-sickness there is little or no naked eye appearance indicating cortical neuronic wasting; and microscopically, although the neurones may be markedly changed in sleeping-sickness, there is comparatively little wasting except in very advanced cases. This absence of wasting of the brain in sleeping-sickness as compared with general paralysis argues in favour of neuronic decay in general paralysis being in great part due to a primary parenchymatous degeneration; although the vascular changes may contribute by inducing a secondary degenerative process. This is not at all unlikely seeing that there is marked capillary and venous stasis in the cortex cerebri. The toxins produced by pullulation of the spirochaetes may have two effects: (1) An action upon the neurone stimulating it to metabolic activity in throwing off side chain molecules and wearing itself out; (2) An action exciting active cellular proliferation of lymphocytes, plasma cells, glia cells and endothelial cells of the capillaries.

THE RELATION OF THE WASSERMANN REACTION TO PARASYPHILITIC AFFECTIONS.

The reaction is due to the presence of a globulin in the blood, the presence of which has been induced by the invasion of the body by the syphilitic organism. Does the reaction only continue to be present in spite of energetic treatment, because the specific organism still remains in the body?

It is a well-established fact that in tabes to some extent and general paralysis still more so, no benefit results from treatment by salvarsan or mercury, and in the latter disease as a rule no permanent effect is produced on the Wassermann reaction.

It may, however, be that we have been led somewhat astray by the results of treatment in asylums where the cases are as a rule too far advanced to be influenced by treatment, or the treatment has not been efficient. For in my hospital practice I have obtained a negative reaction of the blood in a case of well-marked general paralytic insanity, and a great diminution of the lymphocytosis in the cerebro-spinal fluid, together with a lessening of the Wassermann reaction by intensive treatment with salvarsan and mercury. In my practice also I have had three or four cases of so-called parasyphilis, in which the symptoms seem to have been arrested by continuous treatment with courses of mercurial inunction, large doses of iodide being prescribed in the intervals.

THE WASSERMANN REACTION IN GENERAL PARALYSIS.

My assistants, Dr. Candler and Mr. Mann, have examined the cerebro-spinal fluid and blood of several hundred cases of general paralysis, and their results entirely accord with those of Plaut, who obtained a positive reaction

in 97 per cent. of cases (see page 59). A large number of our cases have since died, and the diagnosis in every case where there was a positive reaction was confirmed by post-mortem and if necessary by microscopic examination. Again, the observations by Dr. Topley on my hospital cases of cerebral and cerebro-spinal syphilis compared with tabes and general paralysis entirely conform to Plaut's results. The fluid in cerebro-spinal syphilis more often than not gave a negative reaction.

Most observers admit that the blood gives a positive reaction in a good number of the cases of cerebro-spinal syphilis, but not in all; however, relatively to parasyphilis, the cerebro-spinal fluid less frequently gives a positive reaction.

It is comparatively rare for a specific gummatous meningitis, which usually comes on within a few months or years of infection, to develop later general paralysis or tabes. I can only call to mind two cases on the post-mortem table, but I have observed many cases of apparently cured syphilitic cerebro-spinal meningitis which after several attacks and remissions have died, yet have not shown the characteristic lesions of parasyphilis, although in these cases we had good clinical and pathological evidence of an infection of the cerebro-spinal axis by the specific virus. Moreover, the lesions were random and coarse and the symptoms were accordingly, in correspondence, random and coarse. Again, distinct improvement and temporary, even apparently permanent, cure in some cases followed energetic anti-syphilitic treatment.

If the specific organism is hypothetically presumed to produce no symptoms for a number of years and then induces a meningo-encephalitis or myelitis characteristic of the parasyphilitic affection with secondary degeneration, why does the cerebro-spinal fluid, comparatively to general paralysis, much less frequently and intensely give the reaction in cases of known early syphilitic infection of the cerebro-spinal axis?

I published a striking example of pseudo-tabes in which there was an enormous lymphocytosis of the fluid but never a Wassermann reaction of the cerebro-spinal fluid, the lymphocytosis and the other symptoms all rapidly cleared up with mercurial inunction. I have at present under my care in Charing Cross Hospital a case of basic gummatous meningitis with optic neuritis; the blood gave a marked reaction, the cerebro-spinal fluid a negative reaction.

The cerebro-spinal vessels, although extensively affected by endarteritis and periarteritis, do not as a rule allow the specific globulin which is present in the blood (as the Wassermann reaction of the serum discloses) to pass into the cerebro-spinal fluid. This being granted, how comes it that in 60 per cent. of the cases of tabes and in almost every case of general paralysis (97 per cent.) the cerebro-spinal fluid gives a positive Wassermann reaction. Occasionally

the fluid has given a positive reaction, while the serum was negative, or only slightly positive and the converse ; but as a practical rule it may be stated that when the serum is negative the cerebro-spinal fluid is negative. By analogy with cerebro-spinal syphilitic meningitis we cannot attribute the presence of the complement fixative to leaking of the vessels. If we regard the cerebro-spinal fluid as the special lymph of the brain, then this globulin, which is essential for the reaction, cannot pass through the epithelium of the choroid plexus ; and it is logical to suppose that it comes from the degenerating tissues of the brain and cord according as the case might be one of general paralysis or tabes.

The specific globulin of the Wassermann reaction is therefore in parasyphilitic affections in all probability either derived from the degenerating nervous tissue or is a product of active multiplication of the spirochaetes ; and if this supposition were true the fluid obtained from the ventricles would contain less of the complement fixative than that obtained by lumbar puncture. I have not had the opportunity of verifying the results on the living subject, but my assistants, Dr. Candler and Mr. Mann (see page 71), have tested for me a number of fluids obtained soon after death, drawn off severally by lumbar puncture and direct from the ventricles ; the results in all the 34 instances have been to show that the reaction of the fluid obtained by lumbar puncture was from two to ten times as strong in linking up complement as that from the ventricles. Doubtless, if the fluid could be obtained as it was secreted into the ventricles during life, no specific globulin would exist in it, otherwise it would be found there in all cases of syphilis with a marked reaction.

The deduction is that the complement fixative is being produced within the tissues of the central nervous system ; but is it a product of the neurones which are obviously undergoing degeneration, or is it produced by the perivascular cell infiltration or the neuroglia cells ? Against this explanation is the fact that these latter are in abundance in syphilitic meningo-encephalitis, and yet, as a rule, the fluid, unlike that of general paralysis, does not, as a rule, yield a positive Wassermann reaction.

We have inferentially reduced the pathology of the parasyphilitic affections to a parenchymatous degeneration of the neurone, which is in some way associated with the production of a specific globulin. Under normal conditions the neurones are protected against reacting to poisons because the cerebro-spinal fluid which functions as the lymph of the brain (being a secretion of the choroid plexus) contains none of the toxic substances which may be circulating in the blood ; but in parasyphilis we must suppose that either the specific organism, the spirochaete or some undiscovered possibly intracellular form enters the central nervous system and remains latent for a number of years ;

or more probably in the case of tabes, where there is an elective action on the afferent spinal protoneurones, toxins derived from the specific organisms gain access by the lymphatics, which enter the central nervous system along the vessels and posterior roots of the spinal cord, and acting as sensitising agents stimulate the neurones to throw off the same side chain molecules, specific globulins or complement fixative, which are produced by the cells of the body generally, and which escape into the blood stream. According to the side chain theory of Ehrlich the specific globulins are products of cell metabolism, but the neurones are perpetual elements, incapable of regeneration ; so that if other factors besides the stimulating effect of the spirochaete poison conspire to increase the metabolic activity, nutritional equilibrium will not be maintained and decay will set in ; the retrogressive process attacks first the terminals of the axon, viz., the dendrites and dendrons ; in fact, the degenerative process is an inversion of its growth and development. The process of decay in general paralysis often manifests itself in the earliest stages by an increased irritability and functional activity of the nervous structures, often manifesting itself in a hyperaesthesia sexualis and not infrequently in striking intellectual activity, followed in each case by exhaustion and loss of function. Stimulating chemical products of degeneration or spirochaetal toxin occurring in the cerebro-spinal fluid may account for this increased functional irritability of the neurones prior to their slow or rapid death by destruction of the organised protoplasm. Moreover, toxins, combined with the loss of specific energy and nutritive assimilation of the neurones may stimulate the neuroglia and cells of the ependyma to proliferate, causing the characteristic granulations of the ventricles. The granulations of the fourth ventricle are almost pathognomic of general paralysis ; they are not usually seen in cerebral syphilis ; they are not found in sleeping-sickness. The perivascular infiltration with lymphocytes and plasma cells may own a similar cause or be due to specific syphilitic cyto-toxins caused by the specific reaction of the degenerating cells, or the chemical products of the multiplication of the specific organism escaping into the cerebro-spinal fluid.

I have endeavoured to show that in parasyphilis there is as distinct from syphilis—even when the nervous system is attacked by the specific organism—a participation of the neurones in the reaction to the virus. Normally, the nerve cells are not required to exercise a protective metabolic activity against specific organisms and their toxins, elaborated in the body owing to the inaccessibility of organisms and poisons to enter the cerebro-spinal fluid, the specialised lymph of the central nervous system. Professor Goldman has shown that large quantities of trypan blue may be injected into the blood circulation without its escape into the cerebro-spinal fluid and without

producing nervous symptoms. He has thus injected twice in 24 hours 30 to 50 c.cm. of a 1 per cent. solution of trypan blue without effect ; whilst injection into the subarachnoid space by lumbar puncture of 0·5 c.cm. to 2 c.cm. of a 0·5 per cent. solution of trypan blue caused death of the animal, preceded by acute irritative and paralytic phenomena of the nervous system, which may be associated with coloration of the spinal cord and stem of the brain ; microscopical examination of which showed the neurones all stained by the dye. If likewise, the toxins produced by the spirochaetes find access to the cerebro-spinal fluid, then the effect on the neurones may have similar poisonous effects. In sleeping-sickness we know that the metals arsenic, antimony and mercury are powerless to kill the trypanosomes when once they are found in the cerebro-spinal fluid because they do not pass the choroidal epithelium, and to inject the same direct into the subarachnoid space in sufficient quantity to kill the parasites would kill the patient. These facts may explain why mercury and arsenic have hitherto been unsuccessful in the treatment of general paralysis. Most authorities are now of opinion that if there were no syphilis there would be no tabes or general paralysis ; but are there no other contributory factors ? And if so, what are they ?

CONTRIBUTORY FACTORS IN THE PRODUCTION OF TABES AND GENERAL PARALYSIS.

The dictum of Krafft-Ebing was that general paralysis is the result of "syphilisation and civilisation." There is much evidence to show that contributory factors are required in conjunction with spirochaetal infection to produce general paralysis and tabes. Neisser points to the fact that in countries where alcohol is not consumed general paralysis is not met with. It was, however, said that general paralysis did not occur in a Mohammedan country (*e.g.*, Egypt), though syphilis is very rife among the population. Dr. Warnock of the Abbassiah Asylum, Cairo, has, however, shown that 6 per cent. of the annual admissions are paralytics, which is not below that of many asylums in England. I have already referred to the frequency of tabes in Abyssinia and to Colonel Lambkin's observations of the infrequency of tabes in the recently syphilised population of Uganda. A history of excesses in *Baccho et Venere* is a common result of enquiry regarding the past history of patients suffering with general paralysis and tabes. But then lust and intemperance are not infrequently the first manifestations of a hyper-excitability of the nervous system in general paralysis, and we have remarked that this hyper-excitability may be caused by the toxins of the actively developing spirochaetes.

HEREDITY IN RELATION TO GENERAL PARALYSIS AND TABES.

Charcot, Ballet, Benedikt and Borgherini considered hereditary predisposition to be an important factor in the production of tabes. Redlich, however, attached no great importance to heredity, but Rosenblatt, Fournier, Erb and Gowers looked upon it as a factor of considerable importance. I have not myself had the opportunity of studying heredity in a large number of cases of pure tabes in a satisfactory manner, but I have formed the opinion from a large number of cases of tabes that I have seen, that an ardent sexual temperament which leads to a greater probability of infection is probably a more important factor than any other contributory cause.

My investigation of 3,118 cases of insane relatives who have been admitted to the London County Asylums does not support the conclusions that either hereditary predisposition or the neuropathic temperament play a considerable part in the production of general paralysis. The following is an account of this investigation :—

THE NEUROPATHIC INHERITANCE IN RELATION TO GENERAL PARALYSIS.

It is generally admitted that in pedigrees of general paralysis of the insane, the “neuropathic taint” is not found to anything like the extent that it is in pedigrees of patients suffering from neuroses, psychoses and feeble-mindedness. This is not surprising if we regard general paralysis as an organic disease due, like tabes, to the action of the syphilitic organism.

I have endeavoured to investigate this question by comparative statistics of the incidence of general paralysis occurring in the 3,118 relatives who have been admitted to the London County Asylums, and the incidence in the admissions of the total population : also by comparison of deaths from general paralysis among these two classes of individuals, and I think my results bear out the premise that the neuropathic taint does not enter as a large factor in general paralysis. I will summarise my researches in the subjoined tables.

STATISTICS OF GENERAL PARALYSIS IN RELATIVES.

The incidence of general paralysis in families where two members have been in the London County Asylums is as follows :—

Mother and son.—96 families : 8 families in which general paralysis figured ; in 1 the mother was affected, in 7 the son was affected, and in none were both affected.

Mother and daughter.—157 families : 3 families in which general paralysis figured ; in 1 the mother was affected, in 1 the daughter was affected, and in 1 both were affected.

Father and son.—78 families : 13 families in which general paralysis figured ; in 5 the father was affected, in 8 the son was affected, and in none were both affected.

Father and daughter.—103 families : 12 families in which general paralysis figured ; in 10 the father was affected, in 1 the daughter was affected, and in 1 both were affected.

Brothers.—140 families : 32 families in which general paralysis figured ; in 26 one brother only was affected, and in 6 both were affected.

Sisters.—211 families : 8 families in which general paralysis figured ; none in which both were affected.

Brother and sister.—212 families : 18 families in which general paralysis figured ; in 17 the brother was affected, and in 1 the sister was affected.

Grandparent and offspring.—24 families : 1 family in which the grandparent was a general paralytic.

Collateral pairs.—186 families : 24 families in which general paralysis figured ; in 2 families both male cousins were affected, in 2 families both uncle and nephew were affected, in 5 families one male cousin was affected, in 3 families the aunt alone was affected, in 6 families the uncle alone was affected, in 5 families the nephew alone was affected, in 1 family the niece alone was affected.

As general paralysis is fatal within a year or two of admission, difficulties arise in regard to pairs of paralytics being known, unless one of the pair has been resident since the card system was initiated. Thus, to my knowledge, during the last 15 years there have been three or four cases of husband and wife and of father and son in which one or both of a pair have died at Claybury.

TABLE 1.

Incidence of general paralysis amongst residents in asylum population. 1911 Report. Table E2 :—

---	Males.	Females.	Males and Females.
Total population	8,591	11,475	20,066
General paralytics	334	128	462
Percentage	3·9	1·1	1·5

TABLE 2.

Incidence of general paralysis amongst resident related cases :—

—	Males.	Females.	Males and Females.
Total related cases	616	892	1,508
General paralytics	16	7	23
Percentage	2·6	0·8	1·5

The above Tables 1 and 2 show that whereas in the total resident population of the London County Asylums the proportion of female general paralysis patients to male general paralysis patients is 1·1 to 3·9 per cent., among the resident population of relative case numbering 1,508 it is 0·8 per cent. females to 2·6 per cent. males ; there are, therefore, considerably fewer males and females *pro rata* among the relatives resident.

TABLE 3.

Incidence of general paralysis amongst total deaths occurring in the London County Asylums during the last five years :—

—	Males.	Females.	Males and Females.
Total deaths....	4,126	3,980	8,106
General paralytics	1,385	349	1,734
Percentage	33·5	8·8	21·3

Incidence of general paralysis amongst related cases that have died :—

—	Males.	Females.	Males and Females.
Total deaths....	370	379	749
General paralytics	142	16	158
Percentage	38·3	4·2	21·1

The above Table 3 shows that if we compare the number of deaths from general paralysis during the last five years in all the London County Asylums we find 21·3 per cent. of the total deaths were general paralytics. Our cards of relatives refer to 749 deaths, and of these, as Table 3 shows, there were 158 cases of general paralysis, a total death-rate of 21·1 per cent. Again, comparing the deaths from general paralysis in 2,000 post-mortem examinations at Claybury, I found 23·0 per cent. of the total died from general paralysis ; the slight increase no doubt was due to diagnostic error during

life. The reader will no doubt be struck by the relatively fewer females and the larger number of males *pro rata* among the relatives compared with those of the total population. There is half the percentage of females, and 4 per cent. more males, although the total incidence is almost identically the same (21 per cent.). I would explain this as due to two causes :—

The relatively fewer general paralytic cases occurring among the relatives is probably due to the fact that a considerable number of women admitted to the asylums suffering with general paralysis are derived from a class of female who is more likely to have suffered with syphilis than any other ; they are euphemistically described as of “no occupation.” The prostitute either has no friends to visit her or she is disowned by her relatives, and therefore she is far less likely to appear in the cards of relatives.

The difference among the males is not so great, and may be of no consequence, or the slight increased incidence of general paralysis among the relative cases may indicate that the neuropathic taint does play a small part in the production of general paralysis amongst these cases. The slight increase may also be due to the comparatively large number of brothers affected.

CONGENITAL SYPHILIS AND GENERAL PARALYSIS.

The fact that congenital syphilis may in about 2 per cent. of the cases of general paralysis cause the same pathological conditions to arise at puberty or early adolescence, before intemperance, sexual excess or other exciting causes can contribute, proves to my mind conclusively that syphilis is the essential cause. If it were not for the fact that congenital syphilis, when it attacks the nervous system, is fatal to the foetus or the infant in the vast majority of cases, it is appalling to think what a number of cases of general paralysis might occur in later life. My observations on congenital syphilis in relation to general paralysis point to the fact that latent syphilis of the nervous system is the cause of these cases ; and I have reported cases, and cases have been reported by others, which show that latent syphilis may induce the onset of general paralysis or tabes in adults who have not acquired the disease, even comparatively late in life (Nonne, Christian, Muller). Some cases of general paralysis when they are admitted early to the asylum and all the contributory exhausting and exciting factors are thus removed, live many years. It is therefore probable that a few cases of congenital syphilis may develop general paralysis or tabes early in life, and an arrest of the symptoms take place for years, so that they apparently develop the disease in adult life.

INCIDENCE OF GENERAL PARALYSIS IN THE TWO SEXES.

It is a well-established fact that whereas tabes and general paralysis are met with equal frequency in all grades of society in males, they occur with decreasing frequency in ascending the social scale in females. A very distinguished physician was surprised to hear that females suffered at all with general paralysis. This disparity of incidence of general paralysis of the two sexes is not related to sex, because when the chances of infection are equal as is the case in congenital syphilis, the two sexes are affected in equal numbers by the juvenile form of tabes and general paralysis.

It is calculated that from 3 to 5 per cent. of people who have acquired syphilis subsequently develop tabes or general paralysis. I have no data concerning the incidence of tabes, but it occurred to me that it would be possible to arrive at some conclusion regarding the incidence of general paralysis in the County of London, and also of making some comparison between the various parishes as regards the total admissions to the London County Asylums and the admissions for general paralysis. Inasmuch as the death-rate from this disease nearly corresponds to the admission rate some approximate idea can be formed of the comparative relative incidence of syphilis, if it be assumed that 3 per cent. of the infected subsequently develop general paralysis.

THE INCIDENCE OF GENERAL PARALYSIS IN THE VARIOUS PARISHES OF THE COUNTY OF LONDON.

I asked the clerk of the Asylums Committee to obtain for me information regarding the form of insanity and occupation of all the patients admitted to the London County Asylums. The superintendents were good enough to furnish me with the data required. But I found that owing to the difference of opinion with regard to the nomenclature used by various superintendents for different forms of insanity that the existence of general paralysis was the only reliable information that could be obtained for the comparison of the form of mental disease of patients admitted from the different parishes. Moreover, since the introduction of the Wassermann test doubtful cases of this disease have been far less numerous.

TABLE 4.

Table showing the percentage incidence of male general paralytics among the male admissions from the various London parishes to the London County Asylums during the years 1911-12 :—

1. St. George's, W.	29·0 per cent.	16. Hampstead	14·6 per cent.
2. Whitechapel....	24·2 ,,	17. Lewisham	14·1 ,,
3. Shoreditch	23·2 ,,	18. Camberwell	13·8 ,,
4. Fulham	22·5 ,,	19. Greenwich	13·2 ,,
5. Paddington	20·7 ,,	20. Bermondsey	13·0 ,,
6. Holborn	19·5 ,,	21. Southwark	12·4 ,,
7. St. Marylebone	19·3 ,,	22. St. George's, E.	12·1 ,,
8. Islington	18·6 ,,	23. Mile End	12·0 ,,
9. Kensington	18·4 ,,	24. Bloomsbury	10·3 ,,
10. Wandsworth	18·3 ,,	25. Chelsea	10·2 ,,
11. Lambeth	18·1 ,,	26. Hackney	9·3 ,,
12. Woolwich	17·0 ,,	27. Poplar	9·0 ,,
13. Hammersmith	17·0 ,,	28. Strand	8·9 ,,
14. Westminster	15·4 ,,	29. Stepney	8·8 ,,
15. St. Pancras	15·0 ,,	30. Bethnal Green	4·8 ,,

The number of cases admitted from single parishes suffering from general paralysis are not sufficient to draw any conclusions from, yet I cannot refrain from calling attention to the low incidence of Bethnal Green with a population of 128,282, viz., 1·9 per cent. of the total admissions compared with St. George's-in-the-West with a population of 117,968, where there is 5·2 per cent. of the total admissions due to general paralysis. On account of the numbers I have grouped parishes into east and west ; (a) north, and (b) south of the Thames. Table 5 refers to group (a), Table 6 to group (b).

Showing a comparison of the incidence of insanity and of dementia paralytica in the admissions to the London County Asylums during the years 1911-12, from the parishes north of the Thames, west and east respectively.

[illegible]

TABLE 6.

Showing a comparison of the incidence of insanity and of dementia paralytica in the admissions to the London County Asylums during the years 1911-12, from the parishes south of the Thames, west and east respectively.

Parish.	Population.	Total Admissions, 1911-12.	Admissions per 1,000 Inhab- itants.	Male Admissions.	Male G.P.I.	Percentage G.P.I.	Female Ad- missions.	Female G.P.I.	Percentage G.P.I.
WEST.									
Wandsworth	479,195	727	1.52	300	55	18.3	427	11	2.5
Lambeth	298,126	451	1.51	237	43	18.1	214	9	4.2
Total	777,321	1,178	1.51	537	98	18.3	641	20	3.1
Total percentage G.P.I.	=10.0
EAST.									
Camberwell	261,357	398	1.52	195	27	13.8	203	2	0.9
Bermondsey	125,960	159	1.26	85	11	13.0	74	4	5.4
Lewisham	174,296	197	1.13	78	11	14.1	119	1	0.8
Greenwich	185,688	260	1.40	128	17	13.2	132	5	3.8
Woolwich	127,737	195	1.52	94	16	17.0	101	2	1.9
Southwark	191,951	357	1.86	161	20	12.4	196	9	4.6
Total	1,066,989	1,566	1.46	741	102	13.7	825	23	2.7
Total percentage G.P.I.	=7.9

Table 5 shows on the one hand a relatively high percentage of male general paralytics in the West-end parishes north of the Thames, viz., 17.3 per cent. against 13.2 per cent. for the East-end parishes. On the other hand, the percentage of females is higher in the East-end parishes, 3.4 per cent. compared with 2.5 per cent. in the West-end parishes. The percentage incidence of general paralysis of the total admissions in the West-end parishes is 9.7 against 8.2 East-end parishes.

The average incidence of insanity in these two groups of parishes north of the Thames shows 1.75 West-end group and 1.49 East-end group per 1,000 resident population. Consequently there is a larger incidence of insanity and general paralysis in the richer West-end parishes north of the Thames than the poorer East-end.

Table 6 gives a comparison of east and west parishes south of the Thames ; here we find that the western parishes, Wandsworth and Lambeth have a higher

percentage of admissions with general paralysis, both male and female, than the eastern parishes. The average incidence of insanity in these two groups of east and west parishes is west 1·51, east 1·46 per 1,000 resident.

These two groups south of the Thames, however, do not show quite the same results as the two groups north of the Thames, for the western parishes of Lambeth and Wandsworth show both a higher rate of incidence in males (18·3 per cent.) and females (3·1 per cent.) than the eastern parishes (males 13·9, females 2·7 per cent.); this is not surprising when we consider the class of population living in these two western parishes south of the Thames.

We might ask the question: Why should general paralysis occur more frequently in admissions from West-end parishes than East-end? To answer this question let us first consider the fact that the lower we sink in the social scale the greater is the incidence in women of general paralysis; undoubtedly, the reason for this is the greater number of women who are exposed to infection, and poverty is the most fruitful cause of prostitution.

The incidence of general paralysis in the total female admissions as compared with the total male admissions is one female to seven males. We have seen that the West-end parishes north of the Thames have a higher percentage of males than the East-end parishes, and a lower percentage of females.

TABLE 7.

West-end parishes north of the Thames....	17·3 per cent. G.P. males, 2·5 per cent. G.P. females, equals 7 males to 1 female.
East-end parishes north of the Thames....	13·2 per cent. G.P. males, 3·4 per cent. G.P. females, equals 4 males to 1 female.
West-end parishes south of the Thames....	18·3 per cent. G.P. males, 3·1 per cent. G.P. females, equals 6 males to 1 female.
East-end parishes south of the Thames....	13·7 per cent. G.P. males, 2·7 per cent. G.P. females, equals 5 males to 1 female.

As there are a considerable number of better-class males who develop every year general paralysis and do not come into the London County Asylums, the incidence of seven males to one female in West-end parishes is probably considerably under the mark. The average percentage of male general paralytic admissions annually to the London County Asylums is 15·6 per cent. At Colney Hatch Asylum all the Jews are received, and 15 per cent. of the total admission of male Jews are suffering with general paralysis, so that this about corresponds with the average admission rate.

THE SPECIFIC ORGANISM OF SYPHILIS, THE ESSENTIAL CAUSE OF GENERAL PARALYSIS.

These facts all tend to show that the important etiological fact regarding general paralysis is the relative incidence of syphilis in a population and not drink, mental stress, neuropathic inheritance or other factors. Now that

the specific organism has been found in the brain we shall no longer have an obsession to find causes other than the specific agent. Yet if evidence is wanting to show that conditions of stress play no part in the invasion of the central nervous system by the specific organism of syphilis, there can be no doubt that all causes, *e.g.*, drink, sexual excesses, drugs and insomnia, which depress the specific energy of the neurones can light up and accelerate the progress of the disease. Again, secondary microbial infection, whether by institutional dysentery, broncho-pneumonia, cystitis or bed sores, are according to my experience so frequently associated with convulsive seizures and a consequent destruction of brain substance that it is probable such conditions, by lowering the vital resistance of the tissues, enable the spirochaetes to develop actively. Remissions frequently occur, and vain hopes of cure after a new method of treatment has been adopted are subsequently destroyed only too frequently by relapses. These remissions may, however, occur, when no therapeutic treatment has been adopted. What, then, has caused the cessation of active development of the specific organism? Ehrlich, when showing a preparation of Noguchi at a meeting in Frankfurt-am-Maine, made some remarks regarding the similarity of trypanosome infections and general paralysis; both diseases, he stated, are subject to remissions followed by relapses associated with fever and symptoms. He concluded from his observations on trypanosomiasis in horses that the parasites disappeared from the blood of the horse affected with trypanosomiasis by the generation of anti-bodies; each accession of symptoms was due to the powerlessness of the anti-bodies against a new breed of parasites; and a fresh anti-body had to be produced by the tissues. By analogy he thought the same may happen in general paralysis. Anti-bodies were produced in the nervous system which killed off all the parasites for a time; then new spirochaetes developed which were immune to the anti-body, the unneutralised toxin excited active inflammatory processes and an accession of symptoms. Each relapse is evidence of a fresh development of parasites. The reason spirochaetes are not found in a great number of cases is that the anti-bodies produced tend to spirillolysis. Ehrlich thinks that salvarsan may bring about remissions, but he is doubtful whether a cure can be effected. "General paralysis is no longer to be considered a post-syphilitic affection, but an active infective process."

Probably if we could examine the whole brain we should find spirochaetes in every case, whether convulsions had occurred prior to death or not. This seems probable from the fact that in practically every case of general paralysis the cerebro-spinal fluid contains the eu-globulin of the complement fixative of the Wassermann reaction. This does not come from the blood, as it does not pass through the choroid plexus; it is generated in the nervous tissue

in response to the toxins produced by active proliferation of the spirochaetes. The spirochaetes, even if they occur in foci, do not produce gummatous nodules ; occasionally a gummatous syphilitic brain disease is followed later in life by general paralysis, but it is very rare. We may offer as an explanation of this fact, that either the organism itself differs, or that it has acquired a habit of location in the nervous substance, where it would be uninfluenced by drugs owing to the fact that the nervous substance is irrigated by the cerebro-spinal fluid, and metals, such as arsenic, antimony and mercury do not pass into it ; consequently, they can remain latent there until conditions favour their development. The frontal and central regions of the brain are more wasted in this disease than other parts, and this region corresponds with the distribution of the branches of the internal carotid artery. It is a well-established fact that the aorta in general paralysis is in a majority of cases the seat of atheroma and nodular fibrosis. It is conceivable that the peri-vascular lymphatics of the carotid may convey the specific organism or infective granules from these lesions to the brain ; here they remain latent for years. Another reason why the fronto-central regions are the most wasted is the liability of this region to venous congestive stasis. I long ago pointed out the anatomical condition that caused venous congestion in the fronto-central regions viz., (1) the veins draining this region open into the longitudinal sinus in a direction opposite to that of the current ; (2) the veins run upwards, and therefore gravitation would favour stasis ; (3) the aspiration of the negative pressure in the thorax plays an important part in the cerebral venous circulation ; and the fronto-central area is the most remote from the torcula herophili and the lateral sinuses. Now these conditions which tend to venous stasis, and therefore interference with the oxygen exchange in the frontal lobe, would favour the development of an anærobic organism like the spirochaete.

THE DISCOVERY OF THE SPIROCHAETE IN THE BRAIN.

Evidence is fast accumulating to show that tabes and general paralysis should not be regarded any longer as parasyphilitic or metasymphilitic affections but as "parenchymatous syphilis." The discovery of the spirochaete in the brains in 12 cases out of 70 by Moore and Noguchi, confirmed by further observations and by other workers, has not only forged the last link in the chain of evidence necessary to show that syphilis is the essential cause of general paralysis and tabes, but it has made it necessary to regard the pathology of these diseases in a new light and in future to speak of them as "parenchymatous syphilis." Noguchi has examined 200 brains from cases dying from general paralysis, and 12 spinal cords from tabes dorsalis. He has obtained positive results in 25 per cent. of the cases of general paralysis, whilst only

one of the 12 cases of tabes gave a positive result. He regards general paralysis as a chronic parenchymatous encephalitis. He takes the same view of the therapeutic inefficiency of drugs as I have enunciated.

Marinesco and J. Minea in 1906 published a paper on the absence of spirochaetes in the central nervous system in paralytics and tabetics. They now attribute their failure to discover the organism to the technique employed ; following as they did the Cajal and Levaditi silver methods.

At one time or another I have examined a large number of such silver stained preparations of general paralytic brains without ever having been able to discover undoubted spirochaetes. Nor have I until quite recently ever been able to find them in the cerebro-spinal fluid with the ultra-microscope. Dr. Noguchi, who was kind enough to give me a specimen, informed me that Moore prepared the specimens from the 70 cases first examined, and gave up the search after an infinite amount of pains as hopeless. Possibly he missed them because he expected to find them in the perivascular infiltrations. Noguchi himself was at the point of despair in finding them ; he had examined 70 specimens before he was successful. Afterwards he was able to discover 12 cases out of the 70 with spirochaetes. He found the organisms in all the layers of the cortex except the first. Once he found them in the lower part of this layer. He has never seen them in the pia-mater, which makes him think they have migrated into the cortex. In the latter Noguchi has discovered numbers of spirochaetes diffused about in the nervous tissue ; they were absent in the vessels, and he has rarely found them in the neighbourhood of the great vessels.

Marinesco and Minea state that they have examined 26 cases of general paralysis by various methods of impregnation with silver, and they have only found spirochaetes in great abundance in one case. They believe that they have seen the spirochaetes actually within the nerve cell. They occur in foci in the cortex ; they have not met with them in the pia-arachnoid or in the white matter. They have counted as many as 60 within one field of the oil immersion, and the organisms correspond in all their characters with the spirochaetes found in sections of the liver of congenital syphilitics—an experience which entirely corresponds with my own. These authors are disposed to consider general paralysis as a syphilosis dependent upon the spirochaeta pallida, and it is probable that the inefficiency of treatment, whether it be mercurial or arseno-benzol, is dependent upon the particular resistance that the spirochaetes have gained in the course of their evolution. A photomicrograph of a section kindly sent me by Professor Marinesco, is given in Fig. 1.

Marie, Levaditi and Bankowski have reported three positive results out
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of 30 cases of general paralysis by the silver method. In a more recent publication they claim to have shown that spirochaetes are constantly present in the brains of general paralytics dying in seizures. They emphasise the

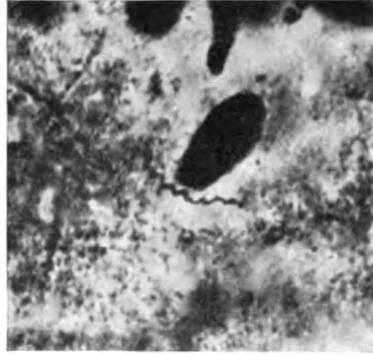


FIG. 1.—Section of brain of general paralysis, stained by the silver method, showing spirochaetes, one in focus; preparation of Professor Marinesco. ($\times 1,550$.)

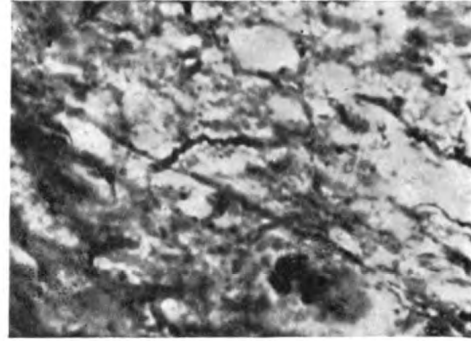


FIG. 2.—Section of brain stained by a silver method from a preparation by Professor A. Marie. ($\times 1,740$.) Many spirochaetes are seen in the field but only one is in focus.

importance of a systematic examination of all the convolutions of the cortex until a positive result is obtained. They do this by sections, by films prepared from an emulsion of the cortex and subsequent examination by the Indian-ink method or the silver method of Fontana. They found spirochaetes in all the seven cases examined. They observe that if one can localise the muscular epileptiform seizures a guide will be formed of a focus of spirochaetes in the neighbourhood of the portion of motor area affected. I show a preparation kindly sent me by A. Marie (Fig. 2). Forster and Tomaszewski obtained two positive results out of four cases in which the material was taken from the patient during life by the Neisser-Pollak puncture method and examined by the ultra-microscope.

NOGUCHI'S EXPERIMENTAL OBSERVATIONS.

Before referring to my own observations I will give a *résumé* of Noguchi's experiments relating to the transmission of the spirochaeta pallida obtained from the brains of general paralytics to the rabbit, and the experimental production of syphilitic encephalitis in this animal.

Noguchi inoculated into the testicles of 36 rabbits the emulsion of six different specimens of brains of general paralytics in the fresh state. At the end of 97 days in one case and 102 days in the other, a small, but typical, induration of the testicle and scrotal skin occurred. In the first case the spirochaetes were few, in the second they were abundant. It is interesting to note how slow was the development as compared with the transmission by infection made with material obtained from a chancre or secondary lesion ;

in the latter case the lesions generally appear after an interval of four to six weeks—rarely two months elapse.

THE EXISTENCE OF THE PARASITES IN THE PARENCHYMA OF THE NERVOUS SYSTEM IN RELATION TO THEIR RESISTANCE TO THE ACTION OF DRUGS.

The above interesting observation of Noguchi may be correlated with the many facts which seem to point to the specific organism that produces general paralysis being either a form which has been modified by the widespread use of mercury or modified by passing through the bodies of individuals who have acquired resistance. Certain it is that the average time after infection in general paralysis and tabes is 10 years, and the signs and symptoms of the disease externally manifest in the form of skin and bone lesions are as a rule either absent, mild or obscure ; whereas in syphilitic brain and cord disease the great majority of the cases occur within the first four years after infection, the greatest percentage occurring in the first and second years. Whereas the signs and symptoms of the latter are coarse, and obvious, and with generally well-marked skin eruptions amenable to treatment, the former—the so-called parasymphilitic, or, as I shall prefer to call them, parenchymatous syphilitic disease—are late (quaternary), and comparatively unamenable to treatment. Is this because they are mercury fast organisms, or is it because they exist in a latent granular or intracellular form in the parenchyma of the nervous system where they cannot be attacked by the drugs such as arsenic, mercury and antimony ? By analogy this does not seem improbable, seeing that in sleeping-sickness, when once the trypanosome has invaded the nervous system, atoxyl and other arsenical and antimonial preparations which were intravenously injected fail to kill the parasite and arrest the progress of the disease. Moreover, there is other evidence in favour of this conclusion. Arsenic is not found in the brain when large quantities of arsenic have been taken in cases of poisoning ; it has not been found in the fluid after injection of salvarsan intravenously. Professor Goldman has shown that the choroid plexus intercepts dyes which have been injected intravenously in large quantities ; *e.g.*, 100 c.c. of a 1 per cent. solution of trypan blue, whereas 1 to 2 c.c. of 0·5 per cent. solution injected by lumbar puncture stains the whole cerebro-spinal axis, penetrating and staining all the neurones. This, as I shall speak of later, has led to the idea of a new method of treatment, not by injecting weak doses of salvarsan or neo-salvarsan intrathecally, for this would be a most dangerous proceeding ; to kill the parasites you would kill the neurones and the patient.

The only case of trypanosomiasis ugandensis that I have heard of as having recovered was a Sikh, whose brain was sent to me for examination. He lived five years after infection and was treated for a long time—18 months—with

atoxyl, then with mercury; for he became intolerant of arsenic and had contracted syphilis. Three years after infection his fluid was examined by Sir David Bruce and found free of trypanosomes, and he showed no signs or symptoms of sleeping-sickness; he died two years later. I examined his brain and found no signs of perivascularitis or neuroglia proliferation—histological changes which were present in every case, 30 in all, that I had previously examined, and which during life had exhibited the characteristic lethargy.

In a recent report from the Nyassaland Protectorate, the principle medical officer has stated that:—"Various treatments have, in the past, been given a trial: (1) atoxyl alone; (2) atoxyl, with intermediate doses of hydrarg. perchlor.; (3) soamin; (4) salvarsan; (5) tartar emetic; (6) dye B.S. In no case was there recovery, and in one or two instances in which some amelioration of the patient's condition was observed, the improvement was merely of a transitory nature. Such slight improvement in symptoms is, however, occasionally noted in patients undergoing no treatment."

These facts show that the presence of the trypanosome in the central nervous system is necessary to produce the meningo-encephalitis characteristic of the disease, although to my mind it is possible that toxins may pass into the central nervous system along perivascular and perineural lymphatics, as Orr and Rows have shown experimentally.

FURTHER EXPERIMENTS OF NOGUCHI.

Noguchi has shown that the central nervous system of monkeys and rabbits is very resistant to syphilitic infection, even when the virus is introduced directly into the cerebral substance. Most animals remain in perfect health during an indefinite period after the intracerebral inoculation of *spirochaete pallidum*. Noguchi conceived the idea that it was necessary to sensitise these animals by repeated intravenous injections with dead and living spirochaetes; this he did for five months. At the end of this time he made an intracerebral inoculation, or subdural insertion of an emulsion of minute particles of testicular syphiloma of the rabbit, rich in spirochaetes. Twelve sensitised and four normal rabbits were employed, all of which remained healthy for two months; then some of the sensitised rabbits showed symptoms. The animals were killed and three of those which had been sensitised showed cerebral changes, not unlike those of a syphilitic meningo-encephalitis.

PERSONAL OBSERVATIONS CONCERNING SPIROCHAETES IN THE BRAINS OF GENERAL PARALYTICS.

Some years ago I attempted to find the specific organism of syphilis in sections of the brain of a number of cases of general paralysis; the sections

were stained by the Levaditi silver method, but after a most diligent search I gave it up. Upon learning of the discovery of Noguchi I re-examined a number of these sections unsuccessfully; and an examination of sections of another set of brains both by the Levaditi method and Noguchi's modification was likewise without success. I therefore resolved to adopt the Indian-ink method applied to an emulsion of the brain soon after removal from the body; and by this method my assistant, Mr. Geary, and I soon obtained apparently positive results (Fig. 3). I say apparently, for it must be admitted that delicate curled tissue filaments might be mistaken for spirochaetes; and unless these spiral forms have been observed in the living state moving on the dark-ground of the ultra-microscope or they are stained by the silver method, convincing proof of their being spirochaetes would be wanting. By the Indian-ink method I obtained spiral forms in 8 out of 11 cases, and by the knowledge which I have obtained by the examination of the fresh brain emulsion on the dark-

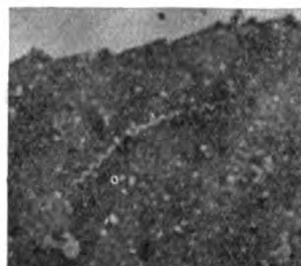


FIG. 3.—Smear of brain of general paralytic, showing spirochaete. Indian-ink method. ($\times 1,550$.)

ground illumination of the ultra-microscope, I am convinced that the forms seen by the Indian-ink method were spirochaetes. Latterly, for this investigation of brains we have employed the dark-ground illumination method and the Fontana* silver method; and we have obtained positive results in 31 out of 47 brains examined. It is impossible to examine the whole of the cortex in a search for foci of spirochaetes, and naturally the question arose, whether clinical or pathological indications would afford a clue to the most likely situations, to find the organism in a series of brains. There is first the probability of association of active multiplication of the specific organism with production of toxins and the onset of seizures. If the seizures are

* FONTANA TRIBONDEAU METHOD.

An emulsion of the brain cortex from a selected spot is prepared by rubbing it up in a glass mortar with distilled water. A thin film is spread upon slide and allowed to dry in the air.

Solution No. 1.—Acetic acid, 1 c.c.; 40 per cent. formol, 2 c.c.; distilled water, 100 c.c.

This solution is poured over the slide and allowed to remain 1 minute and then renewed for 30 seconds.

Solution No. 2.—Acid carbolic, 1 gram; acid tannic, 5 grams; distilled water, 100 c.c.

Pour some of this solution on to the slide and heat until vapour arises or about 20 seconds in the flame of a spirit lamp. This operation is renewed once. Wash in running water for 30 seconds.

Solution No. 3.—Nitrate of silver, 0.25 grams; distilled water, 100 c.c.; liq. ammon. fort., 2 or 3 drops.

This is poured on to the slide to cover the film and heated for 20 to 30 seconds and renewed; then pour off and wash in distilled water for a few seconds and dry with blotting paper.

The preparation can be mounted in Canada balsam and a cover glass placed on the film as it is apt to become decolorised when cedar oil is used.

unilateral it is probable the poison is being produced in the hemisphere opposite to the side on which the epileptiform convulsions are occurring. This idea led me to write an encyclical letter to the superintendents of all the ten London County Asylums, asking them to forward me the brains of patients who prior to death had had seizures. Next it occurred to me that the most likely situations to find the spirochaetes would be those regions which show the earliest naked eye evidence of the disease, namely, the pole and the mesial surface of the frontal lobe, and the frontal end of the limbic lobe; these are regions where congestive venous stasis and adherence of the leptomeninges are first apparent. It was soon found that by far the most satisfactory method, both for rapidity and certainty of demonstrating the existence of spirochaetes, was to make an emulsion of the cortex of the brain from the

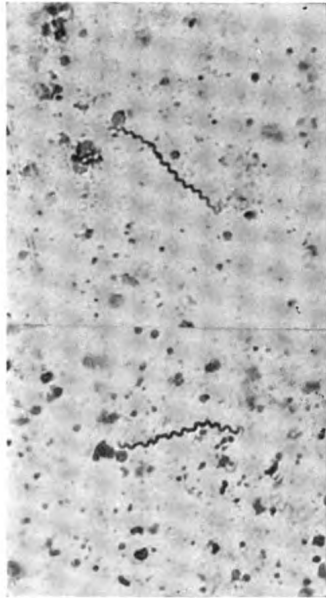


FIG. 4.—Spirochaetes from a smear of brain in case of general paralysis; stained by Fontana silver method. ($\times 1,400$.)



FIG. 5.—Spirochaete in smear of condyloma; stained by Giemsa. ($\times 1,800$.)

regions mentioned, by rubbing up in a glass mortar a little scraping of the grey matter with salt solution or Ringer's fluid, and then examining with the dark-ground illumination. The spirochaetes can easily be seen in the dark-ground; and in a number of instances more or less active movement could be observed. Cases with marked cortical wasting, according to our experience, yielded less satisfactory results than more or less recent cases, with little apparent cortical wasting. Sometimes the organisms were found in a quarter of an hour, sometimes only after a day's search. They seem to be present only in small foci,

for not infrequently a spot a few millimetres away from that in which the organism had been found would yield negative results. The great difficulty of this investigation is that the search for the organism is like looking for the proverbial needle in the haystack ; not finding does not imply non-existence. So far diligent search in regions of the brain other than the frontal have in most instances been unsuccessful, nor have we been able to find the spirochaetes once in brains of patients dying with other forms of insanity. Very often a preparation of brain emulsion showing spirochaetes has been sealed round with paraffin and kept for days and observed at intervals ; numbers of other micro-organisms have been found, but the spirochaetes can still be seen ; and I have observed them moving after the preparation has been kept three days at the temperature of the air. The spirochaetes resemble in form and size those observed in the liver of congenital syphilis, in the scrapings of a hard chancre or condyloma (Figs. 4 and 5). There are, however, great differences in their length and number of coils ; I have observed organisms of varying number of coils, from 5 to 20, and some spirochaetes are much thicker than others ; this

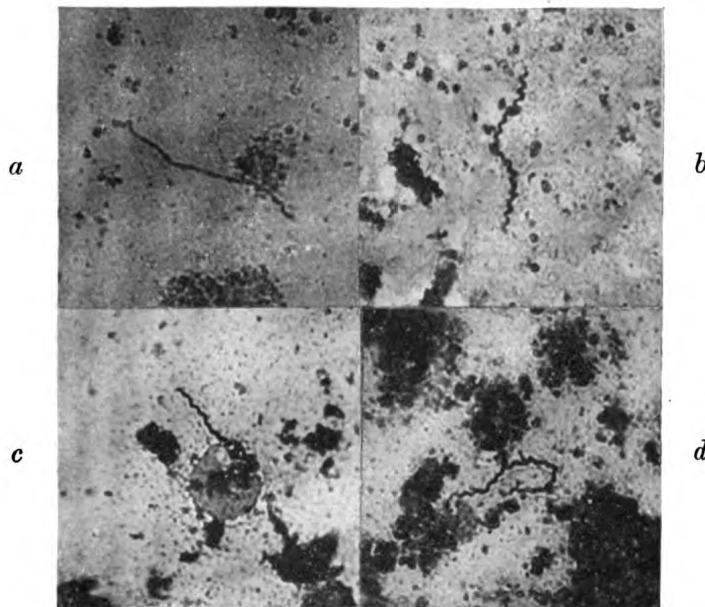


FIG. 6.—Spirochaetes in the brains of general paralytics apparently undergoing modification. Fontana method ($\times 1,400$):—

(a.) Spirochaete showing coil with three spirals, with drawn out extension (without coils) of an apparently granular character.

(b.) Spirochaete with buds attached, a bud being seen as a thickening of a coil in the middle, where it may divide.

(c.) Spirochaete with bud projecting into or out of a cell.

(d.) Spirochaete with numerous coils and buds.

may be due to the fact that they multiply partly by breaking in two, partly by longitudinal fission, indications of which I have often seen in specimens. In preparations which have been kept for some time and where probably the organisms are dead, the spirochaetes may show a spiral form at one end, and the other appears straight or as if the spiral had been pulled out (see Fig. 6A). Again, in these preserved preparations one finds frequently indications of granules and breaking up of the spiral forms into granules. In some of the film preparations stained by Fontana or Giemsa methods, small buds attached by a delicate filament can be seen, or bud-like thickening of the coil of the spiral is not uncommon. It is possible that this marks the place where subsequent transverse division will occur (Fig. 6). These buds may really be due to plasmolysis caused by drying the film.

I have already, on page 8, referred to the observations of Balfour and O'Farrell and those of Leishman, which support the hypothesis of a granule form also of McDonagh and E. H. Ross on the leucocytozoon of syphilis. An interesting case of Eichelberg and Pfortner supports the view that the organism may be latent in the nervous system in general paralysis. Briefly the case is this: A patient who had been infected gave a negative reaction of his blood, and 18 months later he yielded a positive reaction in both the blood and cerebro-spinal fluid; he then had the signs and symptoms of general paralysis.

It is conceivable, therefore, that a latent form may remain dormant in the central nervous system until another factor arises, viz., a loss of durability of the neurones under the influence of two stimulating factors tending to induce excessive metabolic activity in the neurones, which are perpetual cell elements incapable of regeneration. The existence in the circumambient medium of the neurones of chemical substances produced by the specific organism, which causes the specific reaction, as exhibited by the complement fixative of the Wassermann reaction in the cerebro-spinal fluid, would act as a toxic irritant of the neurones. In the case of tabes the toxic substance need not necessarily be produced by organisms in the central nervous system but by foci of organisms in internal parts of the body especially connected by the lymph stream with the posterior columns of the spinal cord. In this way we could explain the fact that only 50 to 60 per cent. of tabetic cases give a Wassermann reaction of the cerebro-spinal fluid. This hypothesis is supported by the experiments of Levaditi and Yamanouchi, which show that a chemical substance excites the cell reaction. They were able to prove this by placing a piece of infected rabbit's cornea into the anterior chamber of the eye of the animal; preceding the invasion of the healthy cornea by the spirochaetes, there was a characteristic cell proliferation.

The more rapid destruction of the nervous elements in general paralysis

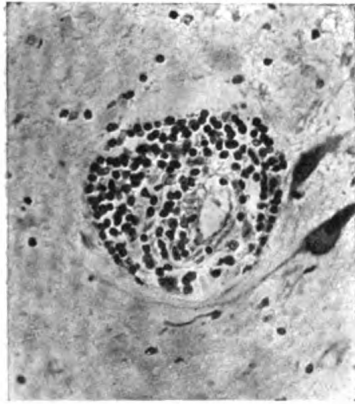


FIG. 7.—Section of the brain from experimental sleeping-sickness showing small blood vessel with perivascular cell infiltration. ($\times 250$.)

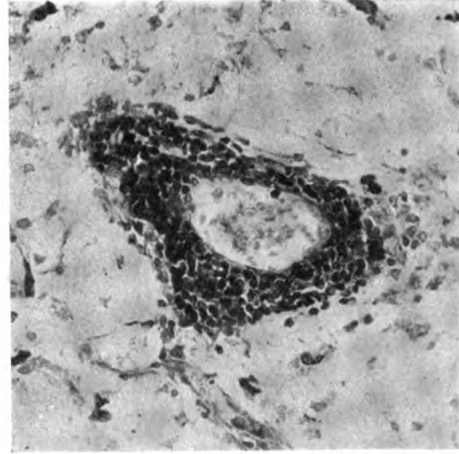


FIG. 8.—Small vessel of the brain in cerebral syphilis showing perivascular cell infiltration. ($\times 250$.)

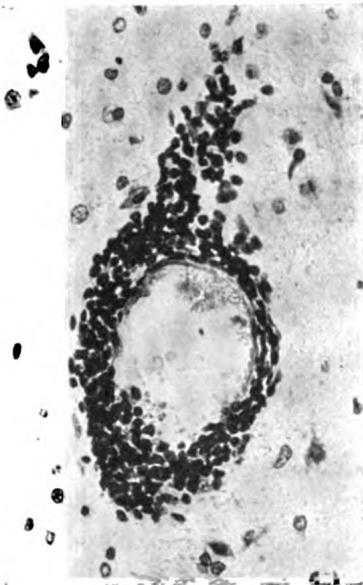


FIG. 9.—Section of the brain of general paralysis showing small vessel with perivascular cell infiltration. ($\times 350$.) This preparation and the two following stained by polychrome blue.

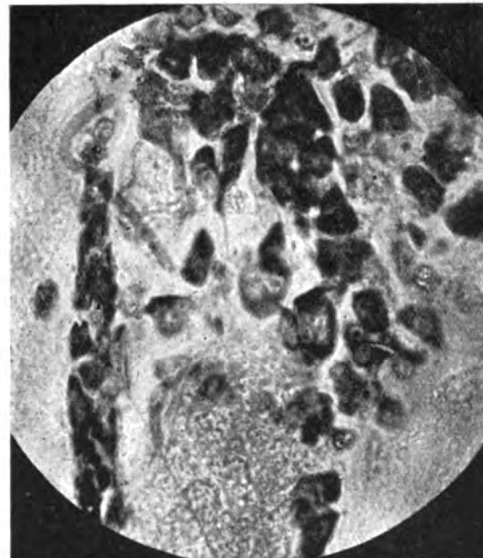


FIG. 10.—Section of brain in general paralysis showing longitudinal section of vessel with active proliferation of plasma cells. ($\times 750$.)

may be correlated with the constant presence of the organism in the central nervous system and the generalised effect of the virus on the whole central nervous system, especially the brain. What part does this virus play in the production of the characteristic perivascular infiltrations with lymphocytes and plasma cells, also the neuroglia proliferation? Similar perivascular appearances and neuroglia proliferation occur in gummatous brain syphilis, general paralysis and in sleeping-sickness (see Figs. 7, 8, 9 and 10). In gummatous brain syphilis, whether localised or diffuse, although there may be profound vascular changes causing interference with the blood supply, yet there is not the profound general wasting of the nervous system generally and of the cortex cerebri in particular, as occurs in all cases of advanced general paralysis. The wasting being in direct proportion to the decay and destruction of nerve cell and fibre systems. In sleeping-sickness where the perivascular infiltration and neuroglia proliferation is as marked as in advanced general paralysis we do not find a proportional wasting of substance and neuronie decay and destruction. Pathological considerations as well as etiological facts, therefore, tend to show that another factor is required of a non-specific nature for the production of general paralysis, viz., conditions and habits of life tending to active metabolism of the nervous system involving mental excitement and stress, with a corresponding deficiency of conditions and habits tending to restoration of neuro-potential, especially worry and insomnia; in fact all those conditions of civilisation which produce neurasthenia, though not essential are probably important contributory factors in determining the onset and progress of paralytic dementia.

RECENT DEVELOPMENTS IN THE TREATMENT OF GENERAL PARALYSIS BY INTRATHECAL INJECTIONS OF SERUM.

In the Oliver-Sharpey Lectures which I delivered at the Royal College of Physicians in April, 1910, I gave many reasons based upon experiments and observations why it seemed probable that the cerebro-spinal fluid functions as the lymph of the brain, I also pointed out that inasmuch as normally it contains no proteids or cell elements, if microbial invasion occurred, it tended to spread rapidly because the fluid normally contained no bactericidal action nor leucocytes capable of combating microbes. These facts have acquired practical application. Flexner and his pupils in different forms of purulent meningitis obtained the best curative results when the therapeutic sera were directly introduced into the subarachnoid space. The proteid reaction and the large and small mononuclear leucocytosis of the cerebro-spinal fluid in tabes and dementia paralytica are indicative of a chronic inflammatory process of the central nervous system, while the presence of the Wassermann reaction

points to the presence of the specific organism as the cause. These late syphilitic inflammatory processes, however, differ from the earlier manifestations of syphilis of the nervous system by the comparative inefficiency of treatment: nevertheless, mercury and iodides are attended with beneficial results, and still more satisfactory results may be obtained by intra-muscular and intra-venous injections of salvarsan. In tabes and even in some cases of general paralysis signs of a chronic inflammatory process may disappear for a time under treatment. Swift and Ellis point out that mercury and iodide often have no effect in tabes, but salvarsan intravenously injected acts more rapidly than mercury and especially does it cause the cytological reaction in the fluid to disappear; it is much more difficult to cause the globulin reaction to disappear completely, also the complement fixative of the Wassermann reaction.

Swift and Ellis were led, therefore, to try the experiment of direct injection into apes of minute doses of salvarsan diluted with the animals own serum; but this treatment caused so marked symptoms of irritation of the nervous system that it was considered inadvisable to try this method on human beings. Neither did similar experiments with neo-salvarsan show that they could employ this mode of treatment. Wechselmann has tried neo-salvarsan in the case of two paralytics and two cases of congenital syphilis, but the results were unsatisfactory. Marinesco treated 13 cases by intraspinal injection of 5 m.g. of neo-salvarsan in 4 c.cm. of saline solution; the results were unfavourable.

The observations of Meirowsky and Hartmann, of Gibbs and Calthrop and of Plaut show that the blood serum of patients who have been treated by intravenous injections of salvarsan when injected subcutaneously into patients suffering with congenital or secondary syphilis had a decided curative effect. Swift and Ellis showed that this salvarsan serum destroyed the spirilla of relapsing fever. They also showed that by the Noguchi method spirochaetes of syphilis can be grown on normal serum-agar, but if salvarsan serum-agar be used the spirochaetes do not grow at all or only slowly. This observation shows that the spirillicidal action of the serum is greatly increased by the salvarsan.

The before-mentioned observations and facts led these two observers to try a new treatment of syphilitic diseases of the nervous system, viz., the injection of salvarsanised sera into the subarachnoid space. The following is the technique they employed:—

One hour after the termination of an intravenous injection of salvarsan 40 c.c. of blood are withdrawn direct into flask formed centrifuge vessels, allowing the blood to clot as it centrifuged. The next day 12 c.c. of the serum

are pipetted off and diluted with 18 c.c. of normal saline. This 40 per cent. serum is then warmed to 56° C. for half an hour. Lumbar puncture is performed and cerebro-spinal fluid is withdrawn until the pressure falls to 30 mm. A calibrated syringe capable of holding 30 c.c. is connected by an india-rubber tube 40 cm. long, with the needle introduced into the subarachnoid space. In order to avoid the possibility of the entry of air fluid is allowed to fill the tube. Serum is poured into the syringe and connection is made with the tube, the serum is allowed slowly to enter the subarachnoid space by the pressure of gravity. By this method any sudden increase of intraspinal pressure is avoided. In their last publication a number of tables are given showing the reactions of the cerebro-spinal fluid before and after treatment by intrathecal injections of serum. Thirty-two patients have been treated with salvarsan and neo-salvarsan serum. They also give a number of tables showing the effect of the treatment upon the cell count, the globulin reaction and the Wassermann reaction. The most marked result is the great diminution in the number of cells present; the Wassermann reaction in 41 per cent. of the cases disappeared, and in nearly all the others was diminished; the globulin reaction was the most persistent. The stronger the Wassermann reaction was at the beginning of treatment the more difficult was it to make the fluid negative. I think it may be assumed that a patient who gives a marked positive reaction in spite of this treatment is probably suffering with tabo-paralysis, and that the complement fixation persists because the spirochaetes existing in the brain are not affected by the serum introduced by lumbar puncture. This treatment is applicable not only to the late forms of syphilis of the nervous system which do not yield to treatment, but also to the early forms.

I recently had under my care a case of gummatous meningo-encephalitis. Infection occurred in February last, and, in spite of intra-muscular injections of salvarsan and mercury, severe cerebro-spinal symptoms set in in September. The cerebro-spinal fluid showed a great abundance of lymphocytes, and a spiral form which resembled a short spirochaete was found in one of the Indian-ink preparations of the centrifuged deposit. As I could not find spirochaetes moving with the dark-ground illumination this is not claimed as convincing proof. The cerebro-spinal fluid, like the blood, in this case yielded a very marked complement fixation. He subsequently received an intravenous injection of 0.4 gram neo-salvarsan with great improvement, but the greatest improvement resulted from intrathecal injections of serum taken one hour after another dose of neo-salvarsan had been administered, subsequent to this the fluid became less positive, and the lymphocytosis disappeared. The serum was tested for arsenic and yielded no result; the legitimate

conclusion being that the action of the serum is due to the presence of anti-bodies in the blood and not to the arsenic. But seeing that I have found that intravenous injections and even intra-muscular injections of salvarsan may convert a positive Wassermann reaction of the fluid in general paralysis into a negative reaction, and thus account for the improvement, it is necessary that the serum of another individual who had received an intravenous injection of salvarsan should be injected into the lumbar subarachnoid sac before it could be claimed that the anti-bodies in the serum were the cause of the improvement. Dr. Swift, of the Rockefeller Institute, said at the International Medical Congress that he had done this with equally satisfactory results. If this be true it would appear that mercury and arsenic are spirillicidal either by causing the development of antibodies or by furthering their spirillicidal action. Dr. George Robertson, of Morningside Asylum, read a paper at the British Medical Association, Birmingham, 1911, recording his observations on the treatment of general paralysis by this serum method. In a more recent paper he, from his experience, does not claim to have attained a cure, and is quite judicious in his statement regarding the effect of this treatment in general paralysis, for he says :—

“Although success has not been obtained there are hopeful indications, for it appears that the disease process, if not suppressed, is at least touched in half the cases. The decrease in the lymphocytosis, the diminution in the intensity of the Wassermann reaction, and its disappearance for over a year in some cases are hopeful signs of the most convincing character.”

Dr. Fisher, of the Rockwood Hospital, Kingston, Canada, who for some months past has been working under my direction at the Pathological Laboratory, Claybury, had the idea of treating general paralysis by this method, and in the spring of 1912, by the kindness of the superintendent, Dr. Ryan, Dr. Fisher took seven cases of advanced general paralysis and rendered the blood negative to the Wassermann reaction by repeated intravenous injections of salvarsan. Then, under rigid antiseptic precautions, he withdrew 15 to 20 c.cm. of blood from the median basilic vein of the patient's arm, placed this in a cool chamber for one hour, separated the clot, and centrifuged the serum for half an hour in sterile tubes. Next he performed lumbar puncture, and withdrew cerebro-spinal fluid of an amount equal to that of the serum to be injected, which is slowly introduced, being kept at the body temperature. The patient is allowed for one hour to lie flat on his back without a pillow, and with the foot of the bed raised. This treatment was repeated every week for the first three months, then every two weeks for the next four months. No untoward symptoms occurred in any of the cases under treatment, and he has learnt that the cases have greatly improved, and apparently there has been an arrest of the symptoms so far.

In an address which I gave at Birmingham on November 14 I pointed out how difficult it is for the serum to arrive at the crannies in the cortex by injecting it by lumbar puncture into the subarachnoid space. I alluded to Goldman's researches with trypan blue, which show that the cortex is unstained when the dye is introduced by lumbar puncture, but is well stained when the dye is introduced by trephining the calvaria. I therefore recommended the introduction of the serum directly into the subdural or subarachnoid space of the cortex. Unfortunately I have not the authority to try this in my capacity of pathologist to the London County Asylums. It is satisfactory, however, to see a communication in the "Comptes Rendus," Seance, December 13, on the Treatment of General Paralysis by Injection of Salvarsanized Serum under the Cerebral Dura Mater, by Levaditi, Marie (de Villejuif) and Martel. They used salvarsanized serum of rabbits. The treatment appeared to provoke an intense reaction in the cerebral meninges, and it was hoped that this reaction would be associated with a specific spirilloidal action and would cause a sterilisation of the cerebral cortex. It is claimed that without doubt the two patients who were thus treated have been benefited, especially the second, which was a less advanced case.

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Statistics regarding General Paralysis in the London County Asylums.

By F. W. MOTT, M.D., F.R.S., F.R.C.P.

These statistics were prepared in order to afford the Royal Commission on Venereal Diseases evidence regarding the incidence of general paralysis as shown by the admissions and deaths in the London County Asylums. During the period under consideration it may be assumed that the population of London has remained stationary at about 4,500,000 inhabitants. The accommodation for the insane provided by the London County Asylums Committee has, however, been more than doubled during this period, from an average daily population of 9,015 in 1893, the London County Asylums have increased the average daily population to 20,240 in 1912.

It will be observed that the number of admissions have by no means increased in the same proportion, for the death-rate and recovery-rate during the latter years have shown a steady diminution ; this has been referred to in another paper—"Is insanity on the increase ? " (see Appendix).

INCIDENCE OF GENERAL PARALYSIS IN ADMISSIONS TO LONDON COUNTY ASYLUMS (1893-1912).

The total yearly admissions of general paralytics to the London County Asylums for the past 20 years as shown by the annual reports of the Asylums Committee have been grouped into four quinquennial periods in the table given below :—

Quinquennial Periods.	Total Admissions.		Total Admissions with General Paralysis.	
	Males.	Females.	Males.	Females.
			Per cent.	Per cent.
1908-1912	9,087	10,174	1,469 = 16·1	268 = 2·6
1903-1907	10,147	11,096	1,399 = 13·8	289 = 2·6
1898-1902	9,002	11,002	1,071 = 11·9	326 = 2·9
1893-1897	7,875	8,893	1,123 = 14·2	294 = 3·3
Total	36,111	41,165	5,062 = 14·0	1,177 = 2·8

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It will be observed that 14 per cent. of the males and 2·8 per cent. of the females admitted to the London County Asylums during the past 20 years were general paralytics.

Regarding the actual number of the male paralytics admitted the numbers show an increase, and if we can assume that the urgency of the case would under any circumstances bring the general paralytic under asylum treatment and that these figures represent the number of cases of general paralysis occurring in the stationary London population, there is no evidence of any diminution of the incidence of general paralysis in London, but rather an indication of a slight increase. Against this inference, however, it must be stated that the modern methods of diagnosis no doubt add to the number of cases of general paralysis, many cases which formerly might not have been diagnosed as such.

With regard to the females, however, the actual numbers of cases have diminished, and assuming the same conditions, the figures seem to indicate a diminution of the incidence of general paralysis in the female London population.

INCIDENCE OF GENERAL PARALYSIS IN THE DEATHS OCCURRING IN THE LONDON COUNTY ASYLUMS (1893-1912).

Quinquennial Periods.	Total Deaths.		Total Deaths with General Paralysis.	
	Males.	Females.	Males.	Females.
			Per cent.	Per cent.
1908-1912	4,208	4,059	1,403 = 33·3	309 = 7·6
1903-1907	3,726	3,649	1,236 = 33·1	323 = 8·9
1898-1902	3,166	3,219	1,031 = 32·5	304 = 9·4
1893-1897	2,619	2,283	988 = 37·7	252 = 11·4
Total	13,719	13,210	4,658 = 34·9	1,188 = 8·9

The above table shows the number of deaths occurring annually, and the number of cases dying of general paralysis in the London County Asylums for the past 20 years, grouped into four quinquennial periods. The figures have been taken from the annual reports of the Asylums Committee.

It will be observed that 34·9 per cent. of the males and 8·9 per cent. of the females dying in the London County Asylums during the past 20 years were general paralytics.

The percentage of male deaths from general paralysis remains at a fairly constant figure, but the percentage of female deaths from general paralysis shows a slight steady decrease.

Owing to the rapidly progressive nature of the disease the number of paralytics admitted during a period is approximately the same as the number that die, for as will be shown later the average life of a paralytic in an asylum is only about 18 months.

These records of deaths are nearly always controlled by post-mortem examinations, and seeing that this disease in the great majority of cases shows characteristic changes in the brain, it may be assumed that the error due to the personal element of the medical officers is in all probability almost a negligible quantity; consequently, we may regard these death records as more accurate than the records of admissions.

During the past 15 years the post-mortems at Claybury have been made by myself or my assistants, and the records have been investigated with the following results:—

INVESTIGATION OF THE CLAYBURY ASYLUM POST-MORTEM RECORDS
(1900–1912).

The records of 1,206 male and 1,267 female autopsies made at Claybury Asylum during the period January 1, 1900, to December 31, 1912, have been investigated.

These were found to include 402 male and 145 female general paralytics, *i.e.*, 33·3 per cent. males and 11·4 per cent. females of the total autopsies, the proportion of males to females being about three to one.

The records of these cases of general paralysis afford the following statistics:—

I.—AGE AT TIME OF DEATH.

Age at time of Death.	Male Paralytics.	Per Cent. of Total Male Paralytics.	Female Paralytics.	Per Cent. of Total Female Paralytics.	Male and Female Paralytics.	Per Cent. of Total.
Under 20 years	3	0·7	1	0·7	4	0·7
20–24 years	5	1·2	4	2·7	9	1·6
25–29 „	18	4·5	9	6·2	27	4·9
30–34 „	42	10·5	22	15·1	64	11·7
35–39 „	90	22·3	33	22·7	123	22·5
40–44 „	75	18·6	30	20·7	105	19·2
45–49 „	70	17·4	16	11·0	86	15·7
50–54 „	52	12·9	16	11·0	68	12·4
55–59 „	24	5·9	9	6·2	33	6·0
60 years and upwards	23	5·7	5	3·4	28	5·1
Total	402	145	547

The above table shows the percentage of the general paralytics dying at the various age periods. There is no marked difference between the figures for the male and female paralytics beyond a slightly greater mortality of the females in the earlier periods. The greatest mortality in both sexes occurs

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between the age period 35 to 44 years ; when 41·7 per cent. of the cases die. This is especially noticeable with regard to the males, for the deaths amongst male paralytics are so numerous that they supply approximately two-thirds of the total male deaths at this age period, and approximately one-half of the total male deaths occurring at the age period 45 to 49 years.

II.—DURATION OF RESIDENCE IN ASYLUM AT TIME OF DEATH.

Duration of Residence.	Males.	Per Cent.	Females.	Per Cent.	Total.	Per Cent.
Under 1 month	22	5·4	8	5·5	30	5·4
1-3 months	66	16·4	13	9·0	79	14·4
3-6 „	55	13·7	18	12·4	73	13·3
6-12 „	73	18·2	29	20·0	102	18·6
1-2 years	99	24·7	27	18·6	126	23·0
2-3 „	35	8·7	20	13·8	55	10·0
3-4 „	19	4·7	13	9·0	32	5·8
4-5 „	9	2·2	8	5·4	17	3·1
Over 5 years	24	5·9	9	6·2	33	6·0
Total	402	145	547

The above table shows the duration of residence in the asylum of the male and female general paralytics. A comparison of the males and females shows that the females live somewhat longer after admission than the males. Taking males and females together, it will be observed that 51·7 per cent. die within one year of admission, and altogether 74·7 per cent. do not survive two years.

The average time elapsing between admission and death of the 402 male general paralytics was 1 year 6 months ; 145 female general paralytics, 1 year 10 months ; 547 male and female general paralytics, 1 year 7 months.

III.—THE INCIDENCE OF ATHEROMA (INCLUDING NODULAR FIBROSIS) OF THE AORTA IN PERSONS DYING WITH GENERAL PARALYSIS COMPARED WITH OTHER FORMS OF INSANITY.

I have long been struck with the frequency with which nodular fibrosis of the aorta and atheroma is found post-mortem in cases of general paralysis. Especially frequent is the existence of a plaque of nodular pearly fibrosis in the first part of the arch of the aorta just above the aortic valve ; this condition of nodular fibrosis which may occur scattered throughout the aorta is the result of a specific inflammatory condition caused by spirochaetal metastasis ; for in early cases of aortitis caused by syphilitic infection the spirochaete can be found. I have not so far been able to find spirochaetes in sections of these plaques but this is not surprising seeing that when a paralytic dies, on an average 10 years have elapsed since invasion of the body by the specific organism. Atheroma is a sign of degeneracy which may be the result of many

causes, of which syphilis is only one. Nodular fibrosis and atheroma are, however, very frequently associated.

The following statistics were collected from the post-mortem records of Claybury Asylum with a view to showing the influence of syphilis as a cause of aortic disease and its consequent direct and indirect effects on the production of bodily disease. It will be observed that the two graphs showing the incidence of disease of the aorta in males and females are strikingly similar. Seeing that the essential cause of general paralysis is syphilis, it may be assumed that owing to syphilis, disease of the aorta occurs at an earlier age and much more frequently in paralytic patients than in the rest of the asylum population, of whom only 10 per cent. have suffered with syphilis.

It is a little difficult to grade the degree of atheroma, because these statistics are based upon the findings of three assistant pathologists who have performed the post-mortems during the last 13 years. Very noticeable was the infrequency of skin lesions indicative of rashes or of gummata compared with the frequency of specific lesions (nodular fibrosis) of the aorta in these post-mortem records of patients dying with general paralysis.

An endeavour has been made to give a statistical expression of the incidence of atheroma (which includes nodular fibrosis) of the aorta in general paralysis as compared with other forms of insanity. The post-mortem records have been carefully investigated and any grade of atheroma noted. In the case of the females a comparison has been made with the same number of cases other than general paralysis dying at the same age periods. With the males, however, this was not possible between the ages 35 to 44, as nearly two-thirds of the total deaths at this age period occurred in cases of general paralysis.

The results are tabulated and graphically expressed below :—

Age Periods.	Males.				Females.			
	Number of G.P.'s.	Number of non-G.P.'s.	Number of G.P.'s with Atheroma.	Number of non-G.P.'s with Atheroma.	Number of G.P.'s.	Number of non-G.P.'s.	Number of G.P.'s with Atheroma.	Number of non-G.P.'s with Atheroma.
			Per cent.	Per cent.			Per cent.	Per cent.
Under 20 years	3	3	2 = 66	1	1
20-24 years	5	5	3 = 60	4	4	3 = 75
25-29 "	18	18	12 = 66	3 = 16	9	9	6 = 66
30-34 "	42	42	32 = 76	16 = 38	22	22	18 = 72	1 = 4.6
35-39 "	90	54	79 = 88	34 = 63	33	33	23 = 70	11 = 33.3
40-44 "	75	36	67 = 89	29 = 80	30	30	27 = 90	17 = 56
45-49 "	70	65	68 = 97	51 = 80	16	16	16 = 100	8 = 50
50-54 "	52	52	47 = 90	46 = 88	16	16	16 = 100	16 = 100
55-59 "	24	24	24 = 100	24 = 100	9	9	9 = 100	9 = 100
60 years and upwards	23	23	23 = 100	23 = 100	5	5	5 = 100	5 = 100

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FIG. 1.—MALES.

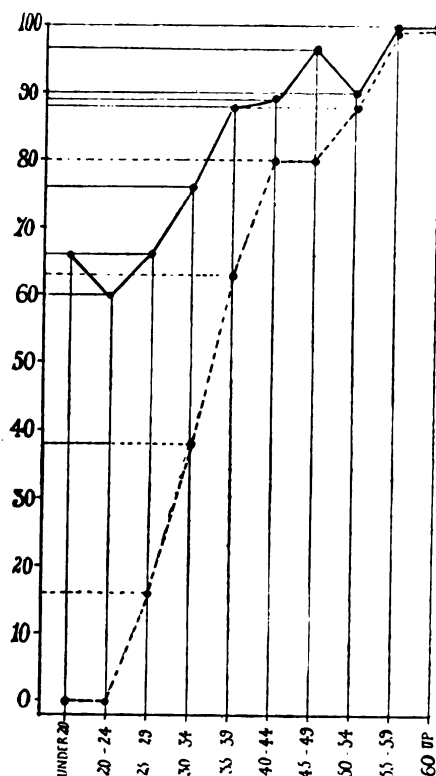
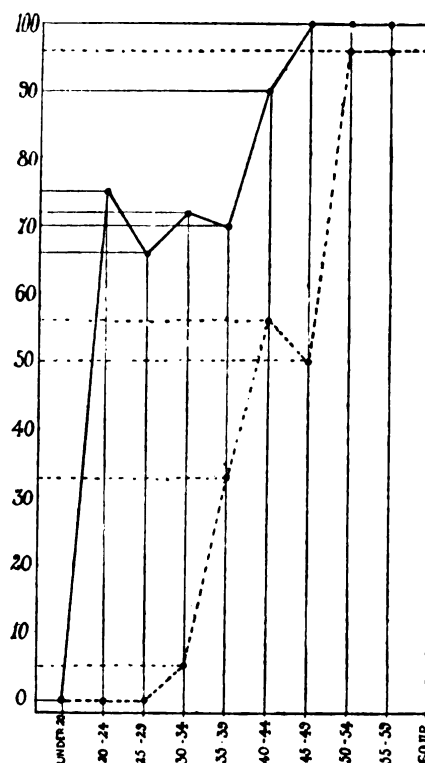


FIG. 2.—FEMALES.



The full line in each graph denotes the percentage incidence of any grade of atheroma and fibrosis of the aorta in male and female general paralytics respectively dying at the various age periods. The dotted line shows the same percentage incidence on cases other than general paralysis.

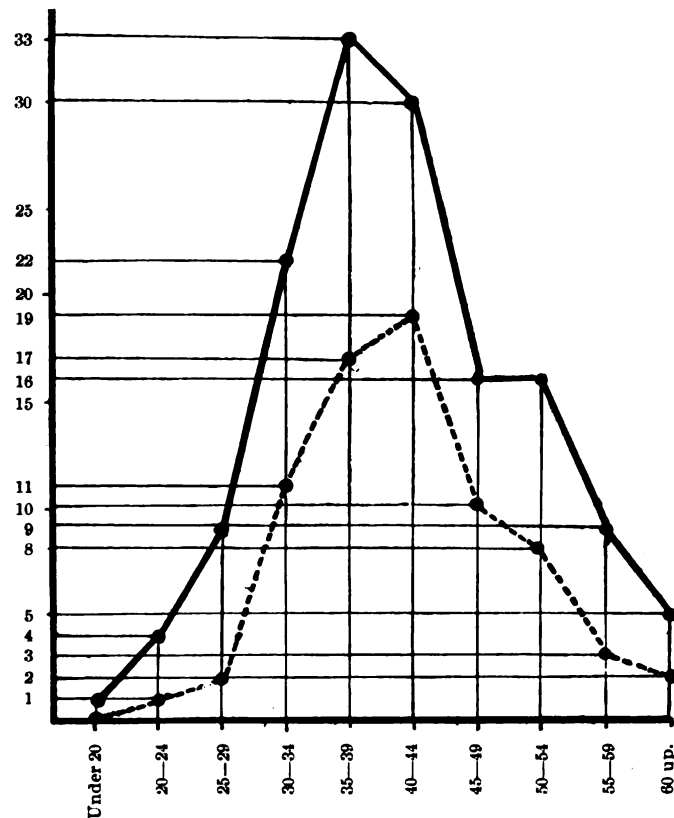
The figures and graphs clearly show the greater incidence of atheroma of the aorta in general paralytics of both sexes at an earlier period of life. Considering only those cases that died under 50 years of age we find that atheroma of the aorta is noted in 86 per cent. of the male and 81 per cent. of the female general paralytics, whereas with other forms of insanity the percentage for the males is 59 per cent. and for females 32 per cent. Moreover, in the case of the general paralytics the atheromatous change is generally of a more advanced nature, and nodular pearly white fibrosis is very common.

The non-general paralytic cases were taken from consecutive autopsies without selection excepting as regards age periods, and they also include a number of cases in which syphilis is obviously manifest.

IV.—THE INCIDENCE OF NON-TUBERCULAR ADHESIVE SALPINGITIS.

The high incidence of non-tubercular adhesive salpingitis in women dying of general paralysis (50 per cent.) as compared with other forms of insanity (6·5 per cent.) shows the probability of a much greater incidence of those social conditions (immorality and prostitution) which are associated with venereal infection. As we may assume that all the female paralytics were infected with the syphilitic organism, it is not surprising that 50 per cent. should show evidence of infection by the gonococcus.

FIG. 3.



The full line shows the number of female cases of general paralysis dying at the various age periods. Total female deaths with general paralysis (1900-1912), 145. The dotted line shows of these same cases the number in which chronic adhesive non-tubercular salpingitis was found post-mortem, in all 73 out of 145 (50 per cent.).

To compare with this figure the records of 400 consecutive autopsies on cases other than general paralysis were investigated. Evidence of chronic (16147)

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adhesive non-tubercular salpingitis was found in 26 instances (6·5 per cent.). Of these 26 cases, 10 were obviously cases in which syphilitic lesions were manifest, as evidenced by :—

Case	1.	Female, aged 50	Gummatous meningitis.
"	2.	" " 52	Gumma of the liver.
"	3.	" " 51	Alcoholic dementia. Suspicious scarring of skin, (?) syphilis.
"	4.	" " 45	Cerebral syphilis with hæmorrhage. Syphilitic aortitis.
"	5.	" " 63	Thoracic aneurism, rupture.
"	6.	" " 62	Alcoholic melancholia. Marked atheroma and fibrosis of aorta. Marked adhesive perisplenitis.
"	7.	" " 47	Cerebral hæmorrhage. Syphilitic endarteritis.
"	8.	" " 63	General arterio-sclerosis. Pearly white fibrosis of aorta.
"	9.	" " 61	Marked pigmentation and scarring of lower extremities.
"	10.	" " 63	Marked pigmentation and scarring of lower extremities.

V.—SIGNS OF SYPHILIS ON THE BODY.

Of the 402 male general paralytics about one-third had suggestive scars on the penis, and 6 per cent. had suspicious scars in the groins.

In 15 per cent. suspicious scarring or pigmentation of the skin was noted, but marked and definite skin lesions indicative of gummata were very uncommon.

The Wassermann Reaction in the Diagnosis of Mental Disorders.

By J. P. CANDLER, M.A., M.D., D.P.H., and S. A. MANN.

It is proposed in this paper to give an account of our experiences of the Wassermann reaction as applied in the Pathological Laboratory of the London County Asylums to the blood serum and cerebro-spinal fluid from various forms of insanity.

Before, however, proceeding to deal with the results obtained it is perhaps advisable to give a brief account of the technique used in this Laboratory for the performance of the test, the reagents employed and the methods adopted for their standardisation.

I.—ESTIMATION OF THE MINIMUM HAEMOLYTIC DOSE.

A series of tubes is prepared containing 0·5 c.c. of a 5 per cent. suspension of washed blood corpuscles and 0·4 c.c. of a 1 in 10 saline dilution of fresh guinea-pig serum and falling doses of the appropriate haemolysin ; each tube is filled with saline to a 3 c.c. volume. The tubes are incubated for one hour, when the minimum amount of haemolysin giving *complete haemolysis* is noted ; this quantity is the *minimum haemolytic dose*. A suspension of sensitised cells is now prepared, each cubic centimetre containing 0·5 c.c. of the 5 per cent. suspension of washed blood corpuscles, an amount of haemolysin equivalent to four times the *minimum haemolytic dose*, and saline to 1 c.c.

II.—ESTIMATION OF THE MINIMUM COMPLEMENTARY DOSE.

Into a number of tubes are introduced 1 c.c. sensitised cells and falling doses of guinea-pig serum diluted 1 in 20 with saline. Each tube is then filled with saline to a total volume of 3 c.c. They are now incubated for one hour, when the minimum amount of guinea-pig serum (complement) giving *complete haemolysis* is noted ; this quantity is the *minimum complementary dose*.

III.—THE WASSERMANN REACTION.

A series of four tubes is used for each test ; into each tube is placed a quantity of guinea-pig serum equivalent to four times the minimum complementary dose (this is generally represented by 0·4 c.c. of a 1 in 10 saline dilution of guinea-pig serum), 0·1 c.c. of a 1 in 5 saline dilution of antigen, a quantity of the cerebro-spinal fluid or inactivated serum to be tested and saline to the constant total volume of 2 c.c.

In the case of the cerebro-spinal fluid the quantities range from 0·8 to 0·1 c.c., and in the case of the blood serum from 0·4 to 0·1 c.c. In special cases larger doses are employed in addition to those mentioned, *e.g.*, 1 c.c. cerebro-spinal fluid and 0·5 c.c. serum. When it is required to estimate exactly the intensity of the reaction a wide range of tests is made containing doses falling to 0·01 c.c. by means of saline dilutions of serum or cerebro-spinal fluid.

The tubes are now incubated at 37° C. for one hour, when 1 c.c. of *sensitised cells* is added to each tube. After shaking, the tubes are returned to the incubator for another 1 to 1½ hours, when the results are read off, and any special cases are placed in the ice chamber for further investigation the next morning.

Control tubes are also put up to show that none of the individual reagents used possess the property of vitiating the accuracy of the test.

We have had considerable experience with both ox and sheep-into-rabbit haemolysin,* and when using sheep haemolysin we have never experienced any difficulty owing to the presence of any natural amboceptor to sheep corpuscles in the serum to be tested.

The serum of the guinea-pig is that collected from the blood of an animal killed the previous evening and placed for the night in the cold chamber. The animal is stunned and its throat cut, and no narcotic is used. We are able to state that out of the large number of guinea-pigs used for the test and killed in the manner mentioned we have only met with two instances in which the serum failed to fulfil the conditions required for the test, and we are able to regard the serum as practically a standard reagent. We are fortunate in being able to keep our animals under ideal conditions, and this may probably account for the fact that we have not met with the variability in the serum experienced by some workers.

The antigen.—Probably the most important point in obtaining a reliable Wassermann test consists in the preparation and standardisation of the antigen,

* As this Laboratory is not licensed under the Act, all the haemolysin used has been supplied by the kindness of the Director of the Lister Institute for Preventive Medicine, to whom Dr. Mott wishes to express his indebtedness.

and to this we drew attention in a previous communication (Proceedings Royal Society of Medicine. "Discussion on Syphilis," 1912).

In this paper we stated that a good antigen obtained from the liver of a syphilitic foetus was not excelled by any other form of antigen, but that it was extremely difficult to obtain.

We have been fortunate in obtaining a good supply of syphilitic foetuses, a few of which supplied us with antigens which fulfilled the most exacting requirements and acted admirably in the test. Samples of these were sent to various workers at their request, and were reported as excellent antigens. But where one efficient antigen was obtained from this material, at least ten extracts had to be rejected owing to their failure to fulfil the standard required.

Owing to this difficulty, we have discarded extracts made from syphilitic material, and now use the mixture of heart muscle extract and cholesterol. From a good experience of this reagent we are able to confirm Drs. McIntosh and Fildes' statements that it answers all the requirements of a "standard antigen." Moreover, it is easy of manufacture, and samples from different sources conform so closely to one another that the production of a good antigen is now simple and economical. It is prepared as follows :—

Heart muscle extract.—Heart muscle obtained from any necropsy and freed from fat is minced and weighed. It is then ground up with silver sand, transferred to a bottle, and absolute alcohol is added in the proportion of 9 c.c. for every gram of heart muscle. The mixture is then shaken on a shaking machine for two hours, filtered and stored in a cool place.

The cholesterol can be easily obtained from any formalin-hardened nervous tissue. The tissue is allowed to dry, the mass is then broken up and cold acetone poured on. After standing over night the acetone solution is decanted and more acetone added. The acetone is distilled off the combined extracts, and the residual crude cholesterol purified by recrystallisation from absolute alcohol.

The antigen consists of—

2 parts of alcoholic human heart extract.

1 part of a 1 per cent. solution of cholesterol in absolute alcohol.

The two constituents are kept separately and mixed before using.

Up to the present time we have not met with a specimen of this "artificial antigen" which has proved inefficient, and bearing in mind the extreme importance of this reagent it is standardised to the following requirements. In the quantity used it must be (1) devoid of all haemolytic and anti-complementary properties; (2) of such antigenic value as to cause prevention

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with the most weakly reacting fluids, to exhibit the utmost grade of intensity of a markedly reacting fluid, and at the same time give a negative reaction with a normal fluid well beyond the dosage used in the test ; (3) it must be of reasonable stability.

With respect to the last demand, we have found that our successful extracts from syphilitic livers remained of remarkably uniform consistency over several months. Regarding the artificial antigen, the cholesterol solution is quite stable, and the heart muscle extract remains of uniform strength for at least two months, but owing to its ease of manufacture, a fresh sample is prepared every four or five weeks.

The antigen in the dilution and dosage usually employed in the reaction is submitted to a test for haemolytic and anti-complementary properties, and it has been the invariable rule to reject at once any antigen that shows the presence of these properties when used in twice the strength employed in the test.

The antigen is then tested with a series of known negative cerebro-spinal fluids and sera and should give a definitely negative result with a minimum of 1 c.c. cerebro-spinal fluid and 0.5 c.c. serum.

It is then tested with a known weakly reacting and a strongly reacting fluid to ascertain whether it gives the maximum prevention of haemolysis in each case, for, as we have previously pointed out, an apparently good antigen may give a maximum prevention of haemolysis with a strongly reacting fluid and yet fail to show a positive reaction with a weakly reacting fluid. Inasmuch as from 20 to 40 cerebro-spinal fluids and sera are frequently tested on one day, it is an easy matter to obtain the material for the tests above mentioned.

Finally, when an antigen has been selected it should from time to time be tested in a manner similar to that described above to make sure that its properties have undergone no definite changes.

Since the Wassermann test has been done in the Pathological Laboratory of the London County Asylums 1,134 samples of serum and 583 of cerebro-spinal fluid withdrawn during life have been examined. The serum of 119 cases and the cerebro-spinal fluid from 205 cases removed after death have also been tested ; the total number of examinations being 2,041.

In 38 cases of general paralysis elaborated comparative tests were made on the cerebro-spinal fluid withdrawn after death from the region of the lateral ventricles and from the spinal canal respectively.

VERIFICATION OF WASSERMANN TEST ON THE CEREBRO-SPINAL FLUID BY
SUBSEQUENT DEATH AND AUTOPSY.

The following figures are given because it will be obvious that it is the most stringent test which can be employed, on which to base statistics as to the accuracy of the reaction as applied to living cases :—

Positive reactions on cases confirmed as general paralysis					
(post-mortem)	191
Negative reactions on cases shown not to be general					
paralysis (post-mortem)	31
Negative reactions shown to be cases of general paralysis					
(post-mortem)	4
Total					226
					Per cent.
Total percentage of accurate results on all cases					98·2
" " " " " in cases of general					
paralysis	97·9

In no case has a positive reaction been found to be other than general paralysis.

With regard to the four cases giving anomalous reactions :—

Case 1.—The cerebro-spinal fluid was negative on the single occasion on which it was examined during life (two months before death). The serum was positive three days before death, and the cerebro-spinal fluid removed post-mortem was found to be positive.

Case 2.—The test on the cerebro-spinal fluid was negative five months before death but lymphocytes were found in the fluid. The serum was not tested. The brain showed the typical characters of general paralysis.

Case 3.—The cerebro-spinal fluid of this case was negative, but the serum was markedly positive when tested at the same time six weeks before death. The case occurred at one of the outlying London County Asylums, and was taken to be one of general paralysis. The brain, however, was not examined microscopically.

Case 4.—The cerebro-spinal fluid of this case examined two months before death was negative to the Wassermann test and no lymphocytes were found in the fluid. It is stated to have been a case of general paralysis. The fluid was sent with several others from one of the outlying asylums of the London County Council, and the majority of them were found on arrival to be undergoing decomposition.

In quoting these four cases in which the test was an apparent failure, it may be mentioned that specimens of cerebro-spinal fluid are sent to the Laboratory
(16147)

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for diagnosis from several of the London County Asylums, and although in several instances the result of the test has not been in agreement with the clinical diagnosis formed on the case, yet it has been found by subsequent post-mortem examination to be accurate. A number of such cases were quoted in a previous paper ("Lancet," November 11, 1911), and their number has considerably increased since that date.

In conclusion we may state that the experience we have had of the test has greatly increased our opinion of its value in all cases presenting obscure clinical features.

THE RESULT OF THE EXAMINATION OF THE SERUM OF CASES OF GENERAL PARALYSIS WITHDRAWN DURING LIFE.

We have also examined the serum withdrawn during life from 186 cases of general paralysis. In 173 of these cases the cerebro-spinal fluid of the patient was also examined.

In 13 cases the serum alone was examined. The material was sent to the Laboratory at various times from several of the London County Asylums, and the diagnosis of general paralysis has been based on the following grounds :—

- (1) Thirteen cases in which the serum alone was examined have since died and have been found post-mortem to be cases of general paralysis.
- (2) In the remaining 173 cases the cerebro-spinal fluid was also positive to the Wassermann test, and there was an excess of lymphocytes in the fluid. A considerable number of these cases have died and the diagnosis of general paralysis confirmed by autopsy. None of these cases that have come to autopsy have been found to be other than general paralysis.

Altogether a positive result on the serum was obtained in 182 cases, but in seven of these the positive result was only obtained after a repetition of the test at a later date. The cases will be referred to later in detail.

The result, therefore, shows that a positive reaction was obtained in 182 out of the 186 cases, a percentage incidence of 97·8 per cent. If, however, we deduct the seven cases which at the first examination gave a negative result the percentage of successful reports is 94·0.

We have already described the main principles upon which the Wassermann test is performed in this Laboratory, and have stated that for each test a minimum of four dilutions is made. This method efficiently checks the technique and enables a quantitative expression of the results to be made; it is, therefore, far more useful and reliable than the single tube qualitative test. We have been able to record changes in the intensity of the reaction

of cases under treatment, and Dr. Wootton (see page 74) using the same method reports a number of similar instances.

We have taken as a unit of complement the minimum complementary dose of our technique (which is generally represented by 0.01 c.c. of pure guinea-pig serum) and express our results as units of complement absorbed per 1 c.c. of cerebro-spinal fluid or serum. In each tube we have four minimum complementary doses of complement, and when any quantity of fluid gives *total* prevention of haemolysis we say that four units of complement have been absorbed. For example, if a tube containing 0.1 c.c. of cerebro-spinal fluid or serum shows complete prevention of haemolysis the reaction is recorded + 40, and similarly for tubes containing other fractions of a cubic centimetre of cerebro-spinal fluid or serum.

This quantitative method has enabled us to show that in general paralysis not only does the serum and cerebro-spinal fluid show marked differences of intensity of reaction in different individuals, but also that the two fluids obtained from the same case may show a very marked comparative difference in their complement deviating properties.

This is shown by the following analysis of the 173 cases of general paralysis in which both the serum and cerebro-spinal fluid were examined. They may be divided into four groups :—

Group I.—In which the reaction of the serum was comparable with that of the cerebro-spinal fluid.

Of the 173 cases examined, 141 fall in this group. In most cases the reaction of both fluids was markedly positive.

Group II.—In which the serum showed the more intense reaction. There were 14 such cases, which are shown with the date and intensity of reaction below :—

No.	Cerebro-spinal Fluid.		Serum.	
1	23.9.11	+ 8	29.12.11	+ 40+
2	2.11.11	+ 8	29.12.11	+ 40+
3	19.10.11	+ 5	27.2.12	+ 20
4	30.3.12	+ 5	7.6.12	+ 40+
5	3.5.11	+ 16	7.6.12	+ 40+
6	19.10.11	+ 5	7.6.12	+ 40+
7	14.6.12	+ 8	19.6.12	+ 40+
8	14.6.12	+ 20	19.6.12	+ 40+
9	2.8.12	+ 8	2.8.12	+ 40+
10	11.2.13	+ 5	16.5.13	+ 20
11	11.2.13	+ 8	16.5.13	+ 40+
12	16.4.13	+ 8	16.4.13	+ 40+
13	12.6.13	+ 8	12.6.13	+ 40+
14	6.3.13	+ 8	30.1.13	+ 40+

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Group III.—In which the cerebro-spinal fluid gave the stronger reaction. The following are the six cases falling in this group :—

No.	Cerebro-spinal Fluid.			Serum.		
1	25.5.11	+	40 ⁺	10.2.12	+	12
2	21.8.11	+	40 ⁺	10.2.12	+	12
3	10.1.12	+	40 ⁺	10.2.12	+	20
4	18.1.12	+	40 ⁺	1.3.12	+	12
5	10.5.12	+	40 ⁺	3.6.12	+	12
6	11.2.13	+	20	6.2.13	+	10

A perusal of the two tables given above will show that in only a few cases was the serum and cerebro-spinal fluid withdrawn from the same individual on the same day and examined at the same time. The fact that an interval elapsed between the examination of the different fluids is likely to raise the objection that little value can be placed on the comparative difference in intensity of reaction between the two fluids. It may be stated, however, that in the 141 cases (Group I) in which the serum and cerebro-spinal fluid showed the same intensity of reaction, the greater proportion of the cases were those in which the two fluids were examined on different days ; further, it will be seen that in some of the 20 cases in which there was a marked difference between the two fluids as regards intensity of reaction, the examination of both specimens was made at the same time.

This difference in the complement deviation powers between the serum and cerebro-spinal fluid of the same individual is a matter of considerable importance. Reference to the tables will show that the reaction in one fluid may be extremely positive while that of the other may be quite slight and liable to be overlooked. Further, as we shall show there may be considerable change in the intensity of the reactions of a fluid when examined at various intervals, and even at times the reaction of the cerebro-spinal fluid or the serum of a definite case of general paralysis may be completely negative.

Group IV.—Lastly, we have met with 12 instances in which the reactions have been specially interesting, and will therefore be described more fully.

Cases 1 to 5 are noteworthy, because with a well marked positive reaction on the cerebro-spinal fluid with lymphocytosis, the first results on the serum were negative, but changed to a positive at a later date.

Case 1.—G. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
17.5.11	+	+ 40 ⁺	29.12.11	—
2.5.12	+	+ 40 ⁺		
3.6.12	+	+ 40 ⁺	3.6.12	+ 20

Died 30.5.13. Autopsy : General paralysis.

Case 2.—S. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
10.11.11	+	+ 40 ⁺	2.2.12	—
			22.5.12	+ 40 ⁺

Case 3.—H. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
25.6.11	+	+ 40 ⁺	10.2.12	—
24.2.12	+	+ 40 ⁺	24.2.12	—*

* Prevention starting with slightly increased dose of serum.

Died 4.6.13. Autopsy : General paralysis.

Case 4.—T. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
26.6.12	+	+ 40 ⁺	24.2.12	—
			26.6.12	+ 40 ⁺

Case 5.—C. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
20.6.12	+	+ 40 ⁺	24.2.12	—
			20.6.12	+ 40 ⁺

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The next two cases show a positive reaction with the cerebro-spinal fluid and a negative reaction on the serum, and later a weak positive serum reaction.

Case 6.—St. (male). Clinical diagnosis :—*

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
26.11.12 9.1.13 +	+ 20 + 8	26.11.12 9.1.13	— + 10

* This case has since died and was found, post-mortem, to be a case of syphilitic meningo-encephalitis with gummatous formation.

Case 7.—W. (male). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
10.4.13	+ 8	26.3.13 30.7.13	— + 10

The following three cases have given a very slight reaction on the cerebro-spinal fluid, and a negative with the serum. In two when the cerebro-spinal fluid was tested later it was found to give a negative result. These cases, however, were, clinically, general paralytics ; one has died, and the diagnosis has been confirmed by autopsy and microscopical examination.

Case 8.—E. (male). General paralysis confirmed by autopsy and microscope :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
24.8.11 24.2.12	+ (?) + (?)	+ 8 —	10.2.12 24.2.12	— —

Case 9.—B. (female). Clinical diagnosis : General paralysis of the insane :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
14.12.11 10.5.12	+ (?) + (?)	+ 8 —	29.12.11	—

Case 10.—R. (female). Clinical diagnosis : Juvenile general paralysis :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
10.5.12	+	+ 5	10.5.12	—

The last two cases, 11 and 12, are interesting, as case 11 gave a positive reaction on the cerebro-spinal fluid but a negative result on the serum, both fluids being tested at the same time ; we were unable to repeat the serum test before the patient died, but the diagnosis of general paralysis was confirmed by autopsy. Case 12, on the other hand, gave a negative result on the cerebro-spinal fluid, and a marked positive reaction on the serum, tested at the same time. This patient also died, and at autopsy the case was stated to be a case of general paralysis, but the brain was not examined microscopically.

Case 11 :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
5.7.12	+	+ 20	5.7.12	—

Case 12 :—

Date.	Cells.	Cerebro-spinal Fluid Result.	Date.	Serum Result.
8.8.12	—	—	8.8.12	+ 40 ⁺

These cases show that while the cerebro-spinal fluid may show a marked positive reaction and lymphocytosis, or a moderate or weak reaction, the serum may be completely negative in the first instance, and may either change to a positive at a later date or remain negative when again examined.

It may be mentioned that in all the cases in which the serum gave a negative result the tests were repeated after further inactivation of the fluid and the use of increasing doses of serum (in some cases up to twice the usual amount), but with a similar negative result except in the instance of case 3, in which some degree of inhibition was observed when a slightly larger dose of serum than usually employed was used in the test.

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The occurrence of cases similar to those described above, in which, in undoubted cases of general paralysis, a serum or cerebro-spinal fluid is found to be negative, and later to change so as to give a slightly positive reaction, is in our opinion mainly responsible for the difference in statistical results which have been published on the Wassermann test in general paralysis.

Moreover, it shows the necessity of making more than one examination of a fluid in doubtful cases, and of the advisability of testing the cerebro-spinal fluid of a doubtful case if a previous examination of the serum has given a negative result.

In cases where the serum is negative and the cerebro-spinal fluid is negative or only slightly positive, the presence of a lymphocytosis in the cerebro-spinal fluid is of very great help in confirming a diagnosis. Boas and others have published their results on the examination of the blood serum in a large number of cases of general paralysis, and have stated that this fluid invariably gives a positive result. Others have only succeeded in obtaining a positive result in from 50 to 70 per cent. of cases of general paralysis. The percentage of positive results in cases of general paralysis obtained at the Claybury Laboratory is 97·9 per cent. on the cerebro-spinal fluid, and from 94 to 98 per cent. on the serum. Although it is probable that both the serum and cerebro-spinal fluid of general paralytics at some time or other during the course of the disease will give a positive Wassermann reaction, we cannot agree with those observers who state that the serum and cerebro-spinal fluid of cases of general paralysis are invariably positive. We are convinced that there are phases in the course of this disease, depending upon some factor as yet unascertained, in which both the serum and cerebro-spinal fluid are negative or so slightly positive to the Wassermann test as to defy detection.

THE VALUE OF THE WASSERMANN TEST AS APPLIED TO THE CEREbro-SPINAL FLUID AND SERUM OBTAINED POST-MORTEM.

It is often very desirable to perform the Wassermann test on serum and cerebro-spinal fluid removed after death in order to confirm diagnosis in cases of suspected general paralysis where no tests have been made during life.

As important cases of this kind came to our notice we considered it advisable to determine how far reliance could be placed on tests made on post-mortem fluids. The account of this work has already been published ("British Medical Journal," March 9, 1912), and our experience since then confirms the conclusions drawn at the time.

Briefly they were as follows :—

1. Out of 112 cases in which the cerebro-spinal fluid was examined post-mortem, a correct result was obtained in 110, or 98 per cent.

In 92 cases the serum obtained post-mortem was also examined, and in six instances only was the reaction obtained considered not to be in accordance with the clinical and post-mortem findings.

2. Our observations led us to consider that the reactions on the blood and cerebro-spinal fluid removed from the cadaver before decomposition has commenced will give reliable results, but we agree with Luksch that decomposition is liable to alter the reaction. This change, however, is not confined to the alteration of a negative to a positive result, but may alter a positive into a negative; and we would point out that decomposition may similarly influence the result of the test on fluids and sera removed during life.

In one typical case of general paralysis in which the cerebro-spinal fluid before death had given a definite positive Wassermann test, a meningitis due to a streptococcic infection was found to have accelerated the final issue. The cerebro-spinal fluid withdrawn post-mortem gave a negative result to the Wassermann test, and the organisms, when afterwards grown in pure culture and inoculated into and grown overnight in a medium consisting of a positively reacting cerebro-spinal fluid, altered the reaction into a negative one.

3. On any case in which a clear cerebro-spinal fluid or a serum showing no haemolysis can be obtained post-mortem, the Wassermann test on these fluids can be taken with reliance.

THE COMPARATIVE INTENSITY OF THE WASSERMANN REACTION OF THE CEREbro-SPINAL FLUID WITHDRAWN POST-MORTEM FROM THE LATERAL VENTRICLES, AND FROM THE SPINAL CANAL, IN CASES OF GENERAL PARALYSIS.

At Dr. Mott's suggestion we have made a quantitative examination of the cerebro-spinal fluid obtained from the lateral ventricles and from the spinal canal respectively, removed post-mortem from 38 cases of general paralysis.

Dr. Mott has suggested that the specific globulin on which the Wassermann reaction has been found to depend in cases of general paralysis, might possibly be derived from the degenerating nervous tissues, and regarding the cerebro-spinal fluid as the special lymph of the brain secreted by the choroid plexus, he suggested that the fluid freshly secreted would be found to contain no complement fixative bodies and that the ventricular fluid should therefore give a much less intense Wassermann reaction than the lumbar fluid.

The following table gives the results obtained in each case in terms of units of complement absorbed per 1 c.c. of cerebro-spinal fluid :—

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Case.	Cerebro-spinal Fluid.		Case.	Cerebro-spinal Fluid.	
	Lumbar.	Ventricular.		Lumbar.	Ventricular.
1	+ 40 ⁺	+ 20	20	+ 400 ⁺	+ 44
2	+ 40 ⁺	+ 20	21	+ 8	+ 4
3	+ 200	+ 66	22	+ 8	+ 4
4	+ 40	+ 8	23	+ 80	+ 40
5	+ 400	+ 40	24	+ 66	+ 57
6	+ 400 ⁺	+ 44	25	+ 80	+ 20
7	+ 100	+ 50	26	+ 20	+ 10
8	+ 80	+ 50	27	+ 40	+ 10
9	+ 100	+ 44	28	+ 20	+ 7
10	+ 20	+ 5	29	+ 10	+ 5
11	+ 44	+ 13	30	+ 400 ⁺	+ 200
12	+ 40 ⁺	+ 13	31	+ 100	+ 44
13	+ 100	+ 50	32	+ 20	—
14	+ 40	+ 13	33	+ 40 ⁺	+ 20
15	+ 20	+ 8	34	+ 40 ⁺	+ 20
16	+ 8	+ 5	35	+ 40 ⁺	+ 20
17	+ 400 ⁺	+ 40	36	+ 40 ⁺	+ 40
18	+ 400 ⁺	+ 200	37	+ 40 ⁺	+ 20
19	+ 133	+ 13	38	+ 40 ⁺	+ 20

NOTE.—It is interesting to observe that in one instance the fluid from the ventricles was negative, and seeing that in every case the fluid obtained by lumbar puncture is greater, generally very much greater in complement fixation than that obtained from the ventricles, and that the possibility of some mixing of recently secreted fluid in the ventricles with that in the subarachnoid space cannot be avoided, these results tend to confirm the hypothesis I have suggested.—F. W. M.

It will be observed that the lumbar fluid was always found to give a more intense reaction than that withdrawn from the lateral ventricles; the intensity varying in nearly every case from twice to ten times as much. Conclusions based on these observations, however, must be given with the reservation that the fluids were removed after death.

The Result of a Series of Wassermann Reactions made on Male Cases in Cane Hill Asylum.

By J. C. WOORTON, M.R.C.S. Eng., L.R.C.P. Lond.

During the past year through the kindness of the Asylums Committee, I have been enabled to work under the direction of Dr. F. W. Mott in the Pathological Laboratory of the London County Asylums.

At Dr. Mott's suggestion I directed my attention to the application of the Wassermann reaction in the diagnosis and treatment of mental diseases, and the following is a preliminary report of the results so far obtained.

Tests have been carried out on the sera and cerebro-spinal fluid of suspected syphilitics, and general paralytics, and on all the male epileptics in the Asylum.

During the last twelve months the blood of every patient admitted to the male side has been examined.

Altogether over 500 sera and fluids and a number of post-mortem specimens have been examined, as follows :—

I.—INVESTIGATION OF BLOOD SERUM IN EPILEPSY.

Age at Commencement of Fits.	Number Examined.	Number Positive Cases.
Under 25	45	3
25-44	8	1
45 and upwards	6	1
Uncertain	7
Total	66	5

Out of 66 epileptics examined, five were found to give a positive reaction on the serum, that is to say, about 8 per cent.

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Male Cases in Cane Hill Asylum.*

In four of the cases, giving a positive serum reaction, in order to exclude the possibility of general paralysis, lumbar puncture was done, and the cerebro-spinal fluid found to be negative. One positive case died before lumbar puncture could be done.

Mercurial inunction was carried out on two positive cases, D and H, and after three months' continuous treatment the sera were again examined and found to be negative.

In one case O, after similar treatment, the reaction was still positive but not nearly so marked, but has now returned to its original intensity.

Another case giving a positive on the serum was placed under treatment, but died before further tests were made.

The following are the details of the non-paralytic cases in which a positive reaction was obtained on the serum and which were submitted to treatment :—

H. Fits since age 18. Teetotal. No family history of insanity, tuberculosis or alcohol.

6.1.05. On admission. Age 25. Pupils unequal. Knee-jerks normal.
Mentally dull and confused.

6.4.05. Developed rash on arms, legs and back. Nothing typical.

9.5.05. Pustular eruption.

11.8.05. Skin well

22.8.12. Serum + 13.

11.9.12. Mercurial inunction commenced.

25.3.13. Lumbar puncture. Cerebro-spinal fluid, Wassermann negative,
no lymphocytosis.

8.7.13. Mercurial inunction ceased.

29.7.13. Serum negative.

27.8.13. Serum negative.

There is no change in the patient's mental or physical condition.

O. Admitted 16.11.1911. Age 52. Married. Had blow over right eye with hammer 16 years ago. Fits began six months later. Alcoholic. Mentally, ill-tempered, querulous, dull. Memory poor. Denies syphilis. Scar in groin.

7.11.12. Serum + 40

9.11.12. Mercurial inunction begun.

8.4.13. Mercurial inunction stopped.

22.4.13. Lumbar puncture, C.S.F., Wassermann negative, no cells.

22.4.13. Serum + 8.

27.8.13. Serum + 40

Fits continue but his general physical and mental condition has improved. It will be observed that the intensity of the reaction diminished with treatment, but since inunctions have been stopped it has gone back to the original intensity, indicating the desirability of further treatment.

D. Admitted 3.1.1911. Age 31. Fits began age 16. Married, one healthy child.

22.8.12. Serum +20.

9.11.12. Mercurial inunction begun.

8.4.13. Lumbar puncture, Wassermann negative, no cells.

8.4.13. Mercurial inunction stopped.

16.4.13. Lumbar puncture, Wassermann negative, no cells.

29.7.13. Serum negative.

27.8.13. Serum negative.

In the above case the positive Wassermann reaction on the serum disappeared as the result of treatment, but there is no alteration in the physical and mental condition of the patient.

II.—THE WASSERMANN REACTION IN GENERAL PARALYSIS.

In the case of general paralytics, the patients admitted to Asylums are usually in a fairly advanced state of the disease; this will account for the high percentage of positive reactions in suspected cases, *i.e.*, out of 69 suspects, 54 gave a positive serum reaction; this supported by the results of clinical examination was considered to clinch the diagnosis; but when a positive serum reaction was obtained, and the clinical signs were not advanced, lumbar puncture was performed, *i.e.*, in 13 cases, 11 of which gave a positive reaction and two negative.

Nine of the diagnosed cases have since been confirmed post-mortem.

G.P.I.	Suspected cases examined	69
	Serums positive	54
	Cerebro-spinal fluids examined	13
	Cerebro-spinal fluids positive	11
	Verified P.M.	9

In several cases, in which there had been a suspicion of general paralysis for some considerable time, a negative reaction enabled a different prognosis being given to the friends; thus in two cases a negative reaction was obtained and the patients were subsequently discharged, without recurrence.

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Male Cases in Cane Hill Asylum.*

The following cases present points of interest :—

(1) M. Age 21. Single. Labourer. Admitted 23.12.11. Regarded on admission as adolescent mania. No external signs of syphilis.

The occurrence of a slight seizure, occasioned a Wassermann test being made ; a marked positive result was obtained on both the cerebro-spinal fluid and serum, with lymphocytosis. A closer inquiry into the history revealed the fact that the mother had numerous children still-born, miscarriages, and children dying in early infancy. There is no family history of insanity.

The diagnosis of juvenile general paralysis was thus confirmed and is in accordance with his present mental and physical condition.

(2) H. This case was admitted first to the asylum 25.2.04, aged 43, he was acutely melancholic, having made several attempts at suicide. He recovered and was discharged six years later. He was readmitted three years later, 24.1.13, with melancholia. At this time and previously there was no suggestion of general paralysis. He denied syphilis and there were no external signs. Within a few months, however, he had a seizure. The Wassermann test then made was markedly positive on both serum and cerebro-spinal fluid, with lymphocytosis. Since this the diagnosis of general paralysis has been confirmed by the patient's typical physical and mental symptoms. Patient now admits having a " sore," when aged 15, shortly after intercourse.

(3) B. Admitted 30.1.09. Age 34. Served in the Army nine years at home and abroad. Last few years carman.

Family history.—Father always a very heavy drinker. Mother insane, age 25, under asylum care prior to birth of patient. Three brothers and two sisters alive and well. Patient had been married five years before admission, no children, or miscarriages. Up to time of marriage he had always drunk heavily and had lived a loose life, but denies syphilis, although admitting frequent risk of infection ; he admits gonorrhœa.

On admission.—Incoherent and unintelligible at times ; memory very defective ; grandiose ideas. Habits wet and dirty. Speech slurred. Inguinal glands shotty. Gait ataxic. Romberg sign marked. Facial muscles tremulous. Pupils small, equal, react to accommodation but not to light.

Since admission.—He has improved mentally and physically. He has had no seizures, and he never had anti-syphilitic treatment.

Wassermann. C.S.F. 11.3.13. Negative, no lymphocytosis.

Serum. 4.3.13. „

Again tested. C.S.F. 27.8.13. „

Serum. „ „ (slight prevention of haemolysis
in top dilution).

At the present time he has considerably improved, his condition being as follows: Pupils small; R. slightly larger than L.; both react sluggishly to light and to accommodation. Knee-jerks normal. Romberg sign absent. Reflexes normal. Gait normal. Speech is not good, many words being clipped, but this may be partly accounted for by the absence of teeth. He is grandiose only as to his muscular development. He is clean in his habits and occupies himself usefully. Mentally is decidedly childish, and is easily provoked.

This case is interesting as being from the first apparently a case of general paralysis but giving negative reactions on the serum and cerebro-spinal fluid. At the present time his condition has improved but the case will be watched, and repeated tests made at a later date.

Since this investigation has been carried out, all wives and children, whenever possible, are interviewed and examined, and if specific infection is indicated the reaction is tried, so that in infected cases treatment may be advised, and these relatives kept under observation.

In this direction Dr. Mott has kindly consented to see any suspected relatives for this purpose, and recently in the case of the wife and children of a general paralytic, by means of examination and the Wassermann test, was enabled to assure them that they were not infected.

III.—THE WASSERMANN TEST, ON THE BLOOD SERUM OF 177 CONSECUTIVE MALE ADMISSIONS.

Since January 1st, 1913, the serum of all cases admitted to the male side has been examined with the following results:—

The blood of 177 consecutive male admissions was submitted to the test and a positive reaction obtained in 55 cases, *i.e.*, 31 per cent. Of these 55 cases, giving a positive Wassermann reaction, 35 were general paralytics.

Excluding general paralytics, a positive Wassermann reaction was obtained on the serum of 20 cases out of 142, *i.e.*, 14 per cent.

Conclusions.—1. The sera of 66 male epileptics have been examined and in five (8 per cent.) a positive result was obtained. In these cases the Wassermann diagnosis indicated anti-syphilitic treatment which has been applied to the patients, with what benefit remains to be seen.

2. The Wassermann reaction has been found of the utmost value in clearing up the diagnosis in cases of suspected General Paralysis, which otherwise might, owing to the suggestive symptoms, have unnecessarily been detained in the Asylum.

3. The examination of the sera of a number of consecutive admissions shows that (including General Paralysis) 55 out of the 177 cases examined

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(31 per cent.) gave a positive reaction. Excluding general paralytics, 20 cases (14 per cent.) out of 142 gave a positive reaction. It is only reasonable to suppose that the wives and children in some of these instances must be infected, and the value of the Wassermann test can be further utilised by the examination of the blood of these relatives wherever possible so that hospital treatment can be advised.

The above figures would indicate that the examination of the sera of all admissions to Asylums is of great importance in diagnosis and treatment.

In conclusion, I would express my indebtedness to the Asylums Committee of the London County Council for the facilities given to me to do this work, to Dr. Mott for his suggestions and encouragement, and to Dr. Candler and Mr. Mann for their unfailing kindness and assistance.

A Study of the Neuropathic Inheritance especially in Relation to Insanity.

By F. W. MOTT, M.D., F.R.S., F.R.C.P.

(Being an address delivered at the opening of the Henry Phipps' Psychiatric Clinic, Johns Hopkins University, Baltimore, Maryland, U.S.A., April 16th, 1913.)

Mr. President, Mr. Phipps, Ladies and Gentlemen, Permit me on behalf of myself and my fellow British workers in psychiatry to thank you for the great honour you have conferred upon British psychiatry by asking one of its representatives to give an address at the opening of this Clinic ; an institution destined in the future to add new laurels to the medical faculty of this great university, which has obtained a foremost place in the world of medical science by spreading the light of research to all parts of the world.

When your distinguished director, Prof. Adolph Meyer, inquired of me the subject of my address I replied : " A study of the neuropathic inheritance especially in relation to insanity." I chose this subject because for the past four years I have been engaged in the study of the relation of heredity to insanity. I feel that the subject is one which still requires an enormous amount of patient investigation before definite conclusions can be arrived at, and the more I work at this subject, the more I am convinced of the wisdom of following the advice of Bacon in his " Advancement of Learning, Divine and Human," when he says : " First therefore in this as in all things practical, we ought to cast up our account, what is in our power and what not ; for the one may be dealt with by way of *alteration*, and the other by way of *application*."

The Investigation of Relative Cases in the London County Asylums.

Four years ago I initiated a card system of relatives who are at present or have been in the London County Asylums. The reason for doing so was to see if the anatomical features of the brain—the organ of mind—showed, like the physiognomy, features of resemblance in the fissures and convolutional

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pattern. Dr. Edgar Schuster has carefully examined and reported on the brain of a mother and daughter and of two brothers, and in his valuable communication (*vide* p. 139) has demonstrated the many points of similarity that exist. Since there is a correlation of structure and function throughout Nature, we may assume that this affords an indication of a resemblance in the raw material of mentality in members of the same family.

Analysis of 3,485 Related Cases (Instances of Two of a Family Insane).

					Pairs.	Cases.
Mother and daughter	174	348
Mother and son	108	216
Father and daughter	112	224
Father and son	83	166
Brothers and sisters	241	482
Two sisters....	227	454
Two brothers	150	300
Husband and wife	76	152
Offspring and grandparents	29	58
Other relationships, collaterals, &c.	224	448
Total					1,424	2,848
160 instances of 3 of a family insane	480
27	"	4	"	"	108
6	"	5	"	"	30
2	"	6	"	"	12
1	"	7	"	"	7
Total					3,485

Total : 3,485 cases made up from 1,620 families.

From a few hundred cases at the commencement of the inquiry the list has rapidly increased until it has now reached nearly 3,500. Each case is indexed on the following card :—

ASYLUM NAMES :

Reg. No.	Name.	Age on First Attack.	Age on Admission.	Date of Admission.	Mental Disorder.	Remarks.

Each card has on it the above information, not only for the patient to whom the particular card belongs, but the same information regarding each insane relative of the family or fraternity. Males have a blue card, females a buff

card. The cards are sent to the various asylums to be filled in with any further information that can be obtained.

The establishment of this card system during the last four years has added greatly to the knowledge of hereditary influence in relation to the causation of insanity among the inmates of the London County Asylums. It has made the statistics published by the various London County Asylums concerning hereditary influence as a cause of insanity much more uniform than was previously the case. It has also markedly increased the influence of heredity in statistics contained in the published reports of the various asylums. This is not surprising seeing that from a few hundred records obtainable at first, the number of cards have increased to 3,500 at the present time.

This system, moreover, has stimulated interest in the subject of heredity in relation to insanity among laymen, and the Asylums Committee were much impressed when they heard that at the present time there are resident in the London County Asylums over 1,500 relatives or persons who were related to one another or had relations previously in the asylums. Still more were they impressed by the fact that there are about 730 persons so closely related as parents and offspring, brothers and sisters, at the present time in the London Asylums. *A priori*; this, to my mind, is striking proof of the importance of heredity in relation to insanity, for we cannot suppose that 20,000 people of the four and a half millions in the County of London brought together from some random cause would show such a large number closely related as 3·6 per cent.

The Committee being so interested, invited me to give a lecture before the County Council on the subject of heredity in relation to insanity. I was glad to do this, because I knew that if the medical officers saw that the Committee were interested in this subject they would be impressed with the fact that it would be to their advantage to assist in the work.

The information necessary to construct these pedigrees was obtained from the friends who visited the patients, but they have been supplemented by further investigation by my assistants and certain medical officers in the asylums.* In constructing these pedigrees every endeavour has been made to make as complete a record as possible for three or more generations. For I recognise the fact that it is far more important to obtain a few complete pedigrees than a number of incomplete ones.

The method of selecting cases for inquiry has been such as to avoid if possible any undue preference being given to any hypothesis or propaganda. The cases have been chosen because the friends were intelligent, numerous,

* The valuable pedigrees obtained by Dr. Wilson White and Dr. Wootton form separate communications (*vide* pp. 99 and 127).

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and able and willing to give as complete an account as possible of the members of the stocks and not because a number of insane relatives were found in a stock.

I soon recognised that the records in the case-books referring to the diagnosis of the form of insanity at the various asylums at different periods of time would form unreliable data for the following reasons: (1) The personal equation of the medical officers; (2) the different classification of insanity and nomenclature adopted in different asylums at different periods of their existence; (3) the change in the diagnosis after admission. Consequently I have only placed reliance on such well recognised conditions as epilepsy and general paralysis of the insane concerning which the personal equation cannot greatly affect the diagnosis, particularly in relation to the latter in which the diagnosis is, in the great majority of cases, controlled by post-mortem examination. I judged that the personal equation, however, could not materially vitiate the data referring to the age at the first attack, discharge from asylum, death, and recurrence of attacks as shown by dates of readmissions.

My statistical observations by the card system of relatives, therefore, mainly relate to the collection and analysis of these data which the personal equation does not materially affect. A criticism has been made that in days gone by fewer people who were insane were admitted to asylums, and this factor would affect the age at the time of first attack of parents and grandparents more than their offspring. The main bulk of the cards, however, refer to parents and offspring admitted to the asylums within the last fifteen years, and I shall give other reasons why this does not materially affect the results.

Anticipation or Antedating in relation to Insanity.—Anticipation or antedating in relation to hereditary disease is represented by the manifestation of the morbid change at an earlier age in members of each succeeding generation. This has been demonstrated by Nettleship in diabetes, and from the study of pedigrees early in my investigations on heredity in relation to insanity, I observed that there was a general tendency for insanity not to proceed beyond three generations, the tainted line of the stock dying out by the inborn tendency to insanity manifesting itself in the form of congenital imbecility, or the insanity of adolescence.

I have found that there is a signal tendency in the insane offspring of insane parents for the insanity to occur at an earlier age and in a more intense form in a large proportion of cases; for the form of insanity is usually either congenital imbecility, insanity of adolescence, or the more severe form of dementia praecox, the primary dementia of adolescence, which is generally an incurable disease. This is statistically shown in the figures regarding the age at the time of first attack in the insane offspring of insane parents.

Statistical data relating to the inheritance of insanity, relating to anticipation.
 —From an investigation of the age at the time of first attack in 508 pairs of parents and offspring (from the records of 464 parents of 500 insane offspring) the following table has been compiled. The figures denote the percentage of cases whose first attack occurred within the given age periods :—

Age Periods.	Father.	Offspring.	Mother.	Offspring.
Under 20 years	1.4	26.2	0.6	27.8
20-24 years	0.4	18.0	3.4	15.7
25-29	1.4	18.0	4.4	18.2
30-34	9.6	13.0	7.8	13.4
35-39	11.5	7.3	9.2	10.0
40-44	9.2	6.4	10.3	5.8
45-49	14.3	6.0	12.0	3.7
50-54	17.5	0.9	12.3	2.4
55-59	13.8	3.7	14.0	1.7
60-64	10.1	11.6	1.3
65-69	5.0	8.8
70-74	4.6	0.4	3.1
75-79	0.4	1.3
80 years	0.4	0.6

The figures are shown graphically in the following diagram, the abscisse representing the age periods and the ordinates the percentage of cases whose age at the time of first attack falls within the given periods.

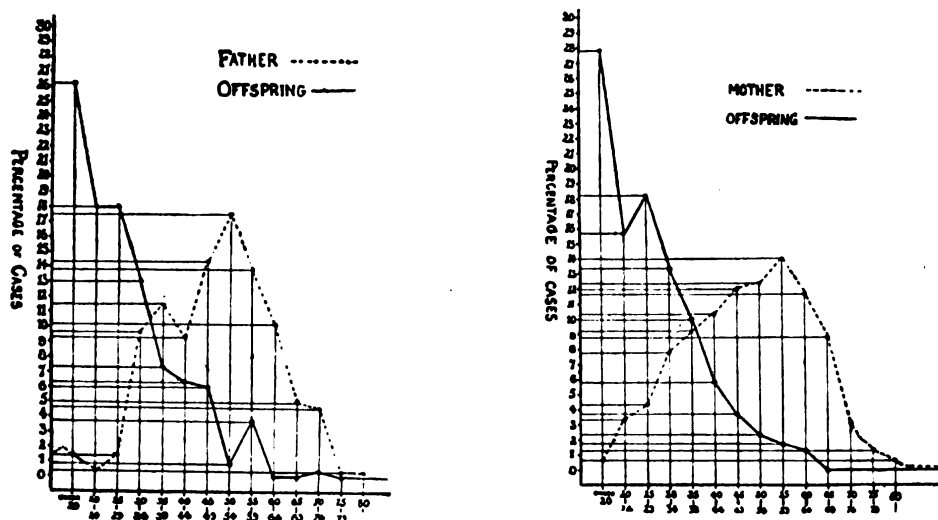


FIG. 1.—A comparison of these two curves will show a notable difference in the dotted line curves of the two parents. The curve of the mothers rises steadily and progressively from 20-55. The curve of the fathers does not commence to rise till after 25; there is a small peak at 35-39. This is the period when general paralysis is most likely to occur. But the main difference in the curves of fathers and mothers is due to the incidence of child-bearing, which causes the steady rise to the climacterium in the maternal curve.

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They clearly show the signal tendency to the occurrence of most of the insanity in the offspring of insane parents at a much earlier age than in the parent ; that is to say, antedating or anticipation is the rule.

Investigating the ages at the time of first attack in the insane offspring of insane parents, I find in the following pairs that 239, or 47·8 per cent. out of 500 offspring, had their first attack at or before the age of 25 years :—

Mother—son	51 out of 118 offspring.
Mother—daughter	81 „ 170 „
Father—son	45 „ 90 „
Father—daughter	62 „ 122 „
Total	239* „ 500 „

* Equals 47·8 per cent.

The following table shows the average age at the time of first attack in the parent and offspring :—

	Parent.	Offspring.
120 pairs, mother—daughter	49·7	29·3
67 „ mother—son	50·2	30·7
76 „ father—daughter	50·1	30·4
51 „ father—son	51·9	33·1
79 parents, 133 offspring in families with more than two insane	47·7	28·7
Total : 393 parents, 427 offspring	49·7	30·0

In addition there were 71 parents whose average age was 49 years at the time of first attack who were associated with imbecile offspring.

Lastly, I find that in 299, or 58·8 per cent. of the 508 pairs of insane parent and offspring, the first attack in the offspring occurred at an age twenty or more years earlier than in the parent ; of these 299 instances 73 of the offspring were imbeciles.

When collateral heredity is studied in a similar manner, the same tendency to the occurrence of anticipation or antedating is shown.

It will be observed that nearly 50 per cent. of these insane offspring had their first attack of insanity at or before the age of 25, and whereas in the case of the insane parents advancing age apparently brings greater liability to insanity, in the case of offspring, with advancing age the liability to insanity tends rapidly to diminish. Now besides the fact that this shows Nature's method of eliminating unsound elements of a stock, it has another important bearing, for it shows that after the age of 25 there is a greatly decreasing liability of the offspring of insane parents to become insane, and therefore on the question of advising marriage of the offspring of an insane parent this is of great importance. Sir George Savage recently said that this statistical proof of mine

accorded with his own experience, and that if an individual who had such an hereditary taint had passed the age of 25, and never previously shown any signs, he would probably be free, and he would offer no objection to marriage.

Pedigrees and statistical data relating to antedating appear to show an intensification and anticipation by a coalescence or crystallisation out of the unsound germinal determinants into a few of the offspring, leaving the germ plasm of the others free. This would not only purify the stock by segregation, but the diseased offspring would be unfit for the struggle for existence and propagation. Marriage of a person who has been in an asylum is discountenanced even among the poor. With the increased accommodation many more imbeciles and insane adolescents are admitted and fewer discharged; consequently, there is a greater tendency by provision of ample asylum accommodation to assist Nature by cutting off the lines of insane inheritance. In putting forward this theory of a germinal segregation by coalescence of similar diseased germinal determinants, I may mention in support of it a statement made by Galton in his great work on natural inheritance, "In the process of transmission by inheritance elements derived from the same ancestor are apt to appear in large groups, just as if they had clung together in the pre-embryonic stage, as perhaps they did."

The material I have collected shows another hereditary tendency pointed out by Darwin, viz., two or more members of the same confraternity affected by a disease exhibit a signal tendency to the onset of the disease at a similar period of life. In a future publication I shall deal with this subject more fully and statistically.

I may say that the examination of pedigrees first led me to regard antedating as one of Nature's methods of eliminating the unfit, and the pedigrees which I have since obtained all tend to support this opinion of the tendency of anticipation or antedating in successive generations. The statistics I have given were brought forward as statistical support to this conclusion. No objection to these statistics on the grounds of selection of cases of poverty of numbers can hold, as the number of instances of insane parent and offspring now reaches nearly 700, and of each case I have authentic notes, and these are taken as reported from a moving population of over 20,000 insane residents in the London County Asylums. But the objections and criticisms raised by an eminent biometrician are valid and require an answer.

Prof. Karl Pearson, writing to "Nature," November 21st, 1912, "On an apparent Fallacy in the Statistical Treatment of 'Antedating' in the Inheritance of Pathological Conditions," criticises on mathematical grounds the evidence of anticipation. I do not feel myself competent to reply to the

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opinion of such an eminent authority on mathematics applied to biometrics, but his criticism does not militate against my conclusions, nor explain away the fact that a large proportion of the insane offspring of insane parents are affected with imbecility or adolescent insanity ; for granting the assumption that there is no antedating at all we might rightly expect the ages at onset of insane offspring of insane parents to be comparable with the ages at onset of all the admissions to the asylums during the same period. This is by no means the case, for amongst the insane offspring there is a far greater proportion affected early in life, as is shown in the following figures and curve .

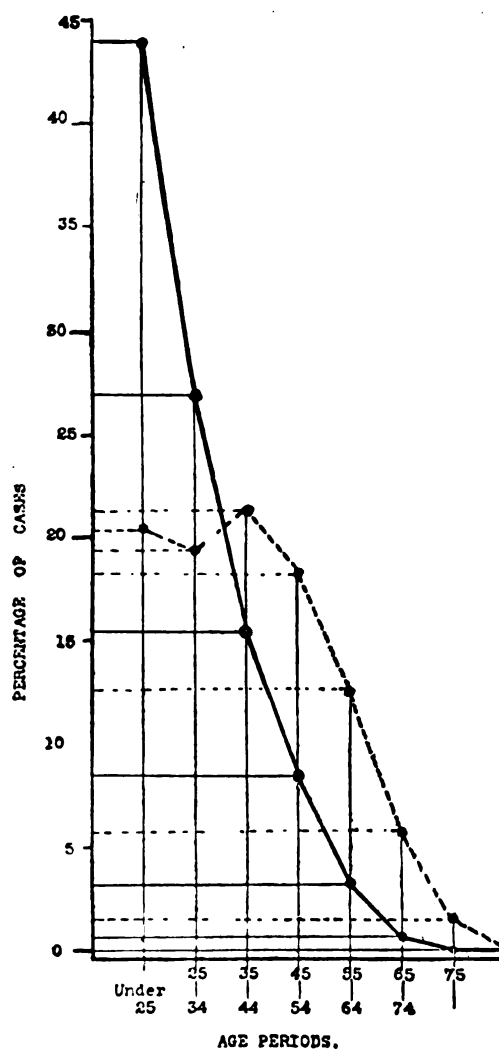


FIG. 2.

Percentage comparison of the age at the time of onset of insanity in the insane offspring of insane parents, and the general admissions to the London County Asylums.

	Males.		Females.		Total.	
	4,482 Direct Admissions during last Four Years.	274 Insane Offspring of Insane Parents.	5,097 Direct Admissions during last Four Years.	389 Insane Offspring of Insane Parents.	9,579 Direct Admissions during last Four Years.	663 Insane Offspring of Insane Parents.
Under 25....	20.0	43.8	20.2	44.2	20.1	44.0
25-34	19.9	27.7	19.9	28.0	19.9	27.9
35-44	21.9	13.8	21.5	16.7	21.7	15.5
45-54	17.7	10.2	18.6	7.4	18.2	8.5
55-64	13.3	3.6	12.4	2.8	12.7	3.2
65-74	5.7	0.7	5.9	0.8	5.8	0.7
75....	1.5	1.6	1.5

41 male	imbeciles out of 274 offspring.		
54 female	„	„	389 „
95 male and female	„	„	663 „

The following points are indicated upon an examination of these tables :—

1. The average age incidence of male and female general admissions for each decade is almost identical. This seems to show that the larger number of females in our asylums is due to accumulation and probably may in great measure be correlated with the fact that the death-rate of males from general paralysis is nearly eight times as great as that of females.

2. The female offspring of insane parents show a slightly greater incidence early in life than the male, the most marked difference being in the early involutional period, 35-44 years.

3. Taking the total offspring or male and female separately, there is a far greater incidence of insanity early in life, especially under the age of 25 years ; and of the 663 insane offspring of insane parents examined 95 or one-seventh were imbeciles.

Before passing on to the investigation of heredity in relation to insanity by the collection of pedigrees, it would be well to state what I mean by the term “ Neuropathic Inheritance.”

The Neuropathic Inheritance.

Temperament and Heredity.—Just as bodily features are transmitted from one generation to another so is temperament. The inborn raw material of character is the complex sum total of the fixed and organised characters of the species and the sex modified by especial racial and family characters. The former are dependent upon complexes of primitive states of feeling and cognition based upon the appetites and desires and the appropriate instinctive reactions for their satisfaction, thereby ensuring the preservation of the individual and the species. The instinctive reactions are associated with concomitant primitive emotional states of feeling and objective manifestations peculiar to the sex and the species. The oldest phylogenetically, they are common to all human beings and are the mainspring of all human action, and this fact has been poetically expressed by Schiller in the following lines :—

Durch Hunger und durch Liebe,
Erhält sich die Weltgetriebe.

The special racial and family characters are of later development, therefore are far less fixed, stable and organised in the nervous system, consequently are more liable to mutation.

A child is born into the world with inborn immutable and mutable characters derived from these genetic sources ; of the importance of the inborn characters in future conduct there can be no doubt ; in proof thereof I need only remind you of Galton's remarkable inquiry into the history of twins. He found that similar twins (developed from one ovum and therefore identical germ plasm) living in a different environment remained similar in temperament and character, while dissimilar twins brought up and living in the same environment remained dissimilar ; these dissimilar twins, however, were the product of two separate ova with dissimilar germs.

Again, Galton, although he formulated a Law of Ancestral Inheritance which appears to be contradictory to the accepted Mendelian Law, certainly recognised that the law only applied to masses of people, and not to individual cases, for he said : " Though one half of each child may be said to be derived from either parent yet he may receive a heritage from a distant progenitor which neither of his parents possessed as personal characteristics." Galton also made a statistical inquiry into the inheritance of good and bad tempers, and his conclusions were that one set of influences tends to mix good and bad tempers in a family at haphazard ; another tends to assimilate them, or that they shall all be good or all be bad ; a third set tends to divide families into contracted portions. He showed that there is always a tendency to revert

to the normal average of the race ; the law of filial regression. The older and more fixed a character is, the more liable is it to this law of filial regression.

A study of the neuropathic inheritance generally accords with Galton's inquiries on tempers. Still the subject which is of paramount importance and interest in heredity now is : Can Mendelism be applied to human characters ? Prof. Pearson says : " No evidence exists of Mendelian proportions occurring in the transmission of obviously human unit characters, *e.g.*, pigment and absence of pigment (albinism)." Prof. Bateson does not affirm that it has been proved for human characters, although he believes that it exists, for he says : " Organisms may be regarded as composed to a great extent of separate factors by virtue of which they possess their various characters or attributes. These factors are detachable and may be recombined in various ways. It thus becomes possible to institute a factorial analysis of an individual." How far such analysis can be carried we do not yet know, but we have the certainty that it extends far and ample indications in supposing that we should probably be right in assuming that it covers most of the features *whether of mind or of body*, which distinguish the various members of a mixed population like that of which we form part.

From such a representation we pass to the obvious conclusion that an individual parent is unable to pass on to offspring a factor which he or she does not possess. Since those individuals only which are possessed of the factors can pass them on to their offspring, so the offspring of those that are destitute of these elements (nulliplex) do not acquire them in successive generations, but continue to perpetuate the type which exists by reason of the deficiency.

Bateson has recently said : " It should be explicitly stated, however, that in the case of the ordinary attributes of man we have as yet unimpeachable evidence of the manifestation of this system of descent for one set of characters only, namely, the colour of the eyes. Moreover, if the evidence as to normal characteristics of man is defective, which in view of the extreme difficulty of applying accurate research to normal humanity is scarcely surprising, there is in respect to numerous human abnormalities abundant evidence that a factorial system of descent is followed." This may be true for certain well defined abnormalities, but as applied to the inheritance of the neuropathic tendency, Mendelian proportions cannot be shown according to my experience, and this is not surprising considering the many forms in which it exists, and even if we take epilepsy, which is perhaps the most easily determinable of all conditions, yet there must be many undiscovered forms which would elude even an expert inquiry concerning the members of the stock affected.

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Dr. Weekes and Dr. Davenport have recently published a remarkable paper on "The Inheritance of Epilepsy," which they claim shows Mendelism in the inheritance of this disease and imbecility. It is a research of great value apart from theoretical considerations on account of the number of pedigrees recorded, but their conclusions appear to me to be open to criticism. Schuster in his review states: "The inheritance of epilepsy and feeble-mindedness can be briefly stated as follows: Such very different conditions as epilepsy and feeble-mindedness must indicate some essential difference in the germ plasm, and the tables which the authors produce show a distinct tendency towards the specific inheritance of these two characters separately; thus the proportion of children who are epileptics born of parents who are both epileptic is higher than when one parent is epileptic and the other feeble-minded and considerably higher than where both are feeble-minded." It seems to me that there is an inherent fallacy in assuming that epilepsy and feeble-mindedness can own the same cause, viz., an absence in the gametes of one and the same germinal determinant or specific factor. It is assumed by these authors that the absence in the zygote of a particular factor or determiner necessary to ensure normal development occasions either feeble-mindedness or epilepsy. Individuals in whom it is absent are called nulliplex, according to the older terminology they would be styled pure recessives or homozygous with regard to the absence of this particular factor. Feeble-mindedness, however, is associated in all my pedigrees with all forms of insanity. Are we to assume that all forms of insanity are due to the absence of this determinant? The authors use the term "simplex" to describe the hetero-zygote. Simplex individuals are said to possess an intermediate mental status, though some are apparently normal. But as pointed out by Schuster it is nowhere precisely stated what are the symptoms of the "intermediate mental states." Now the majority of persons classified in their tables as simplex are either alcoholic or neurotic. Persons who are really normal are called duplex. They have the normal development determiner twice over or are homozygous with regard to its presence. If this theory be correct as Schuster remarks, then when nulliplex mates with nulliplex one would expect to find all the offspring nulliplex. In other words, the children of parents who are both feeble-minded or epileptic should be all feeble-minded or epileptic themselves. Drs. Weekes and Davenport's own tables, however, show this not to be the case, and certainly my pedigrees of epilepsy do not show this. When the Mendelian proportions are not borne out the authors endeavour to explain the fact in various ways, thus when the nulliplex feeble-minded and epileptic offspring are in excess of expectation the excess is accounted for by parental alcoholism. Schuster points out another and more obvious explanation, viz., the manner

in which the material was collected, which had the effect of ensuring at least one epileptic in almost all the fraternities investigated.

"Like tends to beget like," but a collection of statistics and pedigrees merely relating to the existence in members of a stock of certified insanity or fits or weak-mindedness is quite adequate for scientific purposes, as the neuropathic predisposition manifests itself in many different forms, and it is necessary to know something of the temperament and conduct of all the members of a fraternity and as many of the stock as possible to make scientific deductions of value; and this requires time and patient investigation by skilled persons unprejudiced by a propaganda or the desire to prove a theory or the application of a law.

It is very important to seek the first stages and less obvious conditions of degeneration in the stock. Morel, who studied this question more than 50 years ago, pointed out that nervous irritable weakness, the neurotic temperament, neurasthenic predisposition may be the first evidence of degeneration of a stock. Investigation of pedigrees and the experience of the family physician and the alienist specialist shows that the inborn morbid temperament may be manifested in a variety of ways by the behaviour and conduct observed in various members of the stock. The signs of degeneracy which may be exhibited are self-centred narrow-mindedness in religious beliefs, fanaticism, mysticism, spiritism, an unwholesome contempt for traditional custom, social usages and morality, a vain spirit of spurious art and culture, a false self-loving vanity in pursuit of a sentimental altruism, or by eccentricities, anti-crusades and perversions of every kind, the intelligence being generally well preserved; such signs of a morbid temperament are often combined with talent and even genius, especially of the constructive imaginative order; but the brilliant intellectual qualities of a degenerate are generally associated with either a lack of moral sense or of sound judgment and highest control. Nevertheless, these neuropathics often serve a useful purpose in their disregard of tradition and social usages. Time, chance, circumstance and opportunity play an especially important part in moulding and determining the career of members of a neurotic stock; circumstances and environment may favour one member, and he rises on the tide of fortune to an eminent position, whereas another, unfortunate or less fortunate, but with a similar inborn temperament, dies in an asylum or commits suicide in despair.

There can be no question but that the morbid irritability which many men of genius have manifested was but a defect of bodily derangement upon a sensitive mind. Byron in one of his letters said: "I am suffering from what my physician terms gastric irritation. My spirits are sadly depressed. I

have taken a brisk cathartic and to-morrow Richard will be himself again." It is recorded that Voltaire and an Englishman after a long conversation on the evils of this world made a compact to die together the next day. The Englishman appeared and expected Voltaire to keep his promise, but the cynical genius thus expressed the change of his mental attitude: " Ah ! Monsieur, pardonnez moi, J'ai bien dormi, mon lavement a bien opere, et le soleil est tout a fait clair au jour d'hui."

In searching for the neuropathic tendency there are many possibilities of missing the inborn factor of a neurosis or psychosis, though a careful inquiry be made, even when aided by intelligent co-operation of the friends. It is necessary to inquire into the family life and conduct of the members of a stock to find the neuropathic taint. How often may it be observed that an apparently sound stock may in reality be unsound. Successful men in the eyes of the world may be really degenerates ; not infrequently so-called self-made men form the first step in the process of degeneration. The selfishness and meanness or the cunning, avarice and moral guile by which they have succeeded in amassing a fortune for their children to spend selfishly is the first evidence of degeneracy ; but whereas the parents to gratify their selfish desires succeeded by work and abstemiousness, the children, possessing the same selfish instinct with no need to work, and supplied with abundant wealth, acquire vicious habits and criminal propensities, and not infrequently terminate their careers in the madhouse or prison. At the same time I do not wish to lay too much stress upon inborn criminality. Imitation and suggestion play a large part, for an inborn virtue under evil surroundings may lead to the worst forms of vice. When pedigrees are constructed showing in successive generations numbers of criminals, paupers and lunatics, are we quite sure that there has not been a continuance in successive generations of those social conditions that lead to crime and pauperism and the exciting causes of the insanity ? I have often found in the collection of pedigrees the association of insanity and suicide in a stock preceded by, or associated with, the existence of individuals possessing the melancholic, suspicious, brooding, self-centred, hypochondriacal temperament ; and it is not uncommon for suicide of one or more members of the stock in successive generations to occur. Associated with these temperamental evidences of degeneracy of a stock may be chronic alcoholism, dipsomania, hysteria, hypochondriasis, exophthalmic goitre, neurasthenia, psychasthenia, migraine, petit mal, or neuroses of an epileptic character, often unrecognised because not manifesting fits of the major form of the disease.

The Creation of the Neuropathic Inheritance in Healthy Stocks.

If my premise is true that Nature is always trying to end or mend a degenerate stock by natural selection and sexual selection aided by anticipation—or the signal tendency to the occurrence of insanity at an earlier age in the offspring of insane parents—there must be causes at work which either tend to revive a latent neuropathic inheritance or to develop the first stage of degeneracy by the cumulative effects of an unfavourable environment in previously healthy stocks. The great difficulty is to determine what are previously healthy stocks.

We have seen that the neuropathic inheritance is much wider than is generally supposed, and includes many temperamental conditions and masked forms of neuroses and psychoses which might easily escape recognition without very complete and careful investigation. Consequently unsuitable mating may easily be overlooked as a cause of epilepsy or insanity appearing in a family. This was so in the case of the pedigree of two cousins which is shown in Fig. 3. Again, there may be latent insanity in a stock and by not searching

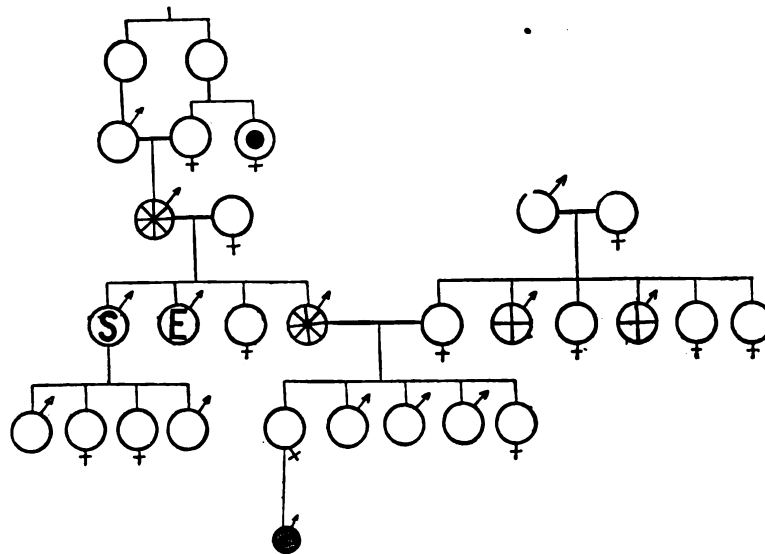


FIG. 3.—A pedigree, illustrating the marriage of first cousins. A genius was the result; he married a healthy woman, and their family consisted of an eldest son, a suicide; a second son, an epileptic; a daughter, healthy, unmarried; and a son, a genius. This man was a genius but had an extremely well-balanced mind; all his five children are healthy in spite of collateral inheritance on both sides.

Circles with black centres—*physically unsound*. Circles in quadrants—*alcoholism*. Circles in octants—*genius*.

far enough back in a pedigree drink *per se* may be assigned as the cause of epilepsy or insanity appearing in a family tree, Fig. 4. The following pedigree

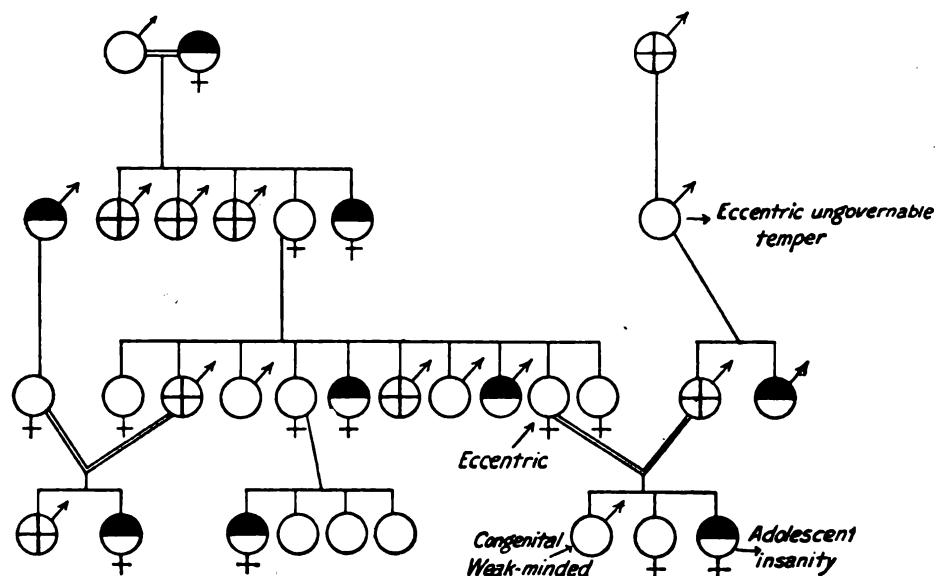


FIG. 4.—Pedigree of a well-to-do family with marked alcoholism (circles in quadrants) and insanity (half-black circles).

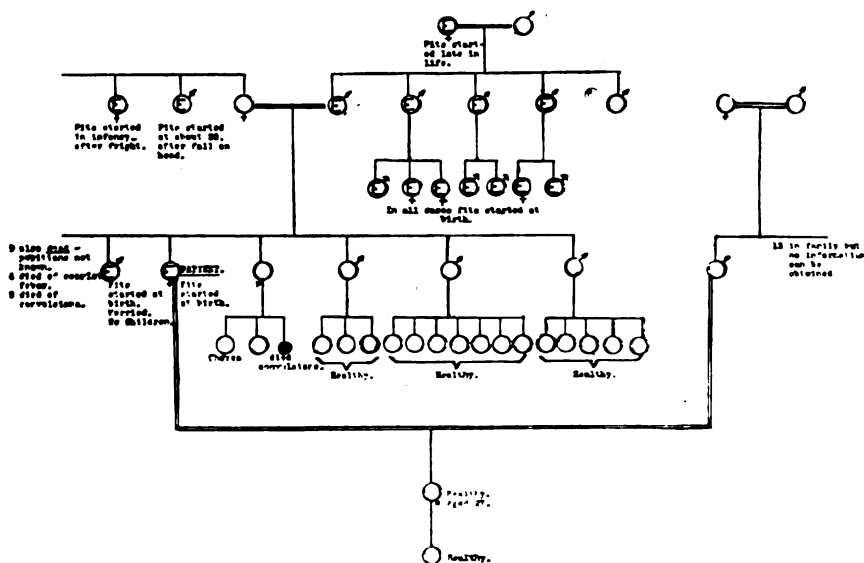


FIG. 5.—The above pedigree shows the transmission and apparent elimination of a marked epileptic taint. The pedigree commences with the grandmother of the patient, whose fits commenced late in life. Four of her children were epileptics, and one, now dead, was not. According to the history three of these married and begat between them seven children, all epileptic, whose fits commenced at birth. The eldest, however, married a female who was not an epileptic but came from an epileptic stock, shown by the fact that she had a brother and a sister subject to fits. There were numerous children from this marriage, and of the six surviving, two were epileptics from birth (one of whom is the patient) and the remainder are healthy, also their children, with the exception of one suffering from chorea. The epileptic patient married into an apparently good stock, one healthy female child was the result; and this child has reached adult age and is now the mother of a healthy infant.

(Fig. 5) is of interest as showing how uncertain may be the results of mating even in the case of the most heritable of all forms of nervous and mental disease—epilepsy. The most unpromising mating in this pedigree seems to have ended in a few generations in the elimination of the unsound elements. In the next pedigree, Fig. 6, however, we find that the epileptic taint may skip a generation,

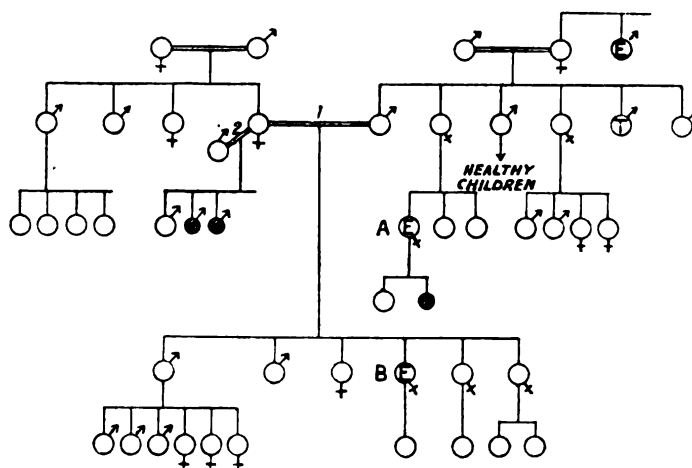


FIG. 6.—This pedigree is of interest in showing the appearance of epilepsy in two members of a stock after it had missed a generation. All other members of the stock were mentally unaffected. One of the offspring of one of the affected members (A) died from injuries received while the mother was in a fit; while the only child of the other affected member (B) was the result of seduction by her stepfather.

so that we are never sure of the absence of a latent tendency which may be revived by unpropitious mating or by some acquired conditions involving the general health of the body and especially the brain. The next pedigree (Fig. 7) is of interest in showing healthy and intelligent progeny from a family in which all the surviving members are or have been insane. But we cannot predict yet what may happen to these children as only few of them have arrived at adult age. The puerperium seems to have been in the case of all the four females the exciting cause of the insanity.

One of the questions of greatest interest in the study of heredity in relation to insanity is this, can the germ plasm long subjected to poisoned conditions of the blood undergo a pathological mutation affecting the functions of that most complex of all organs—the brain? The only organ which could vary with advantage to the individual and the species, and therefore not fixed and stable as regards its highest and latest developed functions is the brain, the organ of mind. Poisons may be introduced into the body from without for long periods of time, as in the case of chronic alcoholism and lead poisoning. Poisons may be engendered in the body as the result of the invasion and growth

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of parasitic organisms, *e.g.*, syphilis and tuberculosis. Can these race poisons so affect the germ plasm as to cause a loss of specific energy of the germ cells so that they are affected as regards the determiners of the higher and later

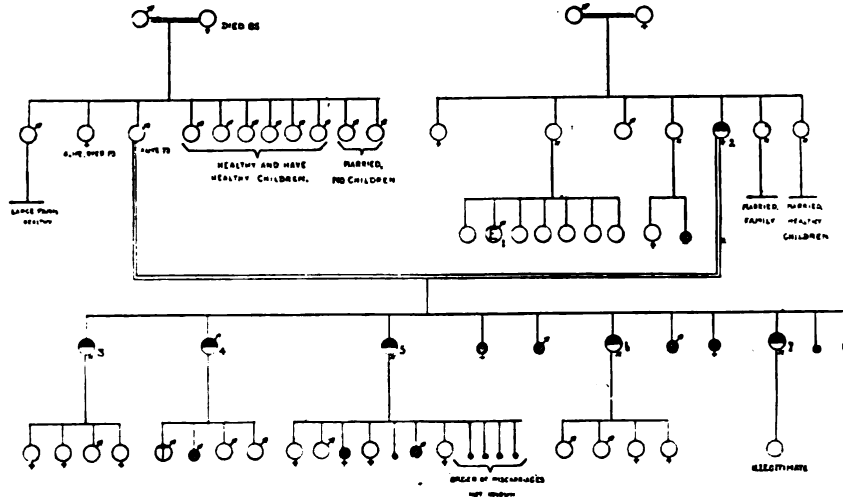


FIG. 7.—The above pedigree is of interest in showing healthy and intelligent progeny from a family in which all the surviving members are or have been insane. The father of this family is living (aged 72) and his brothers and sisters are normal, and show longevity and fecundity, their children being healthy. On the mother's side there is no insanity noted, except in the case of (1) who commenced to have fits at the age of 4, these were severe and continued until he died at the age of 38.

(2) The mother; she first became insane at the age of 38, at the time of the birth of (7); from this time until she was aged 54 she was in and out of asylums, but from 54 until the age of 66 she remained outside, when she was again admitted to the asylum and remained there until she died at the age of 72.

(3) Is now in asylum. First certified at the age of 45, but she had had three attacks previously and these were associated with the birth of her children. Her four children, however (eldest 19, youngest 10), are healthy and above the average intelligence.

(4) Is now in asylum. Admitted to the asylum at the age of 45, had previous attacks but was not certified. Cause stated to be worry due to desertion by his wife. His first child died aged 17 of consumption; the second died, aged 3, from complication arising from rickets. The two other children are alive and healthy, aged 18 and 14 years respectively.

(5) One attack of insanity at the age of 30, in asylum for three months following the birth of her fifth child. The surviving children are healthy, clever and above the normal order of intelligence.

(6) First attack at the age of 24, following birth of first child, two other attacks since associated with child-birth. Her eldest child, aged 11, had convulsions from 15 months to 3½ years of age, but is now healthy and clever. The remaining three children are bright and healthy.

(7) First attack at age of 19, associated with birth of an illegitimate child. Had three attacks since and is now in asylum.

developed functions of the brain? It is extremely difficult to show by pedigrees that a blood poisoning can produce *per se* a mutation of the germ plasm, causing epilepsy and insanity to arise in a healthy stock and be

transmitted. It is first necessary to prove by careful investigation that there is no latent epilepsy or insanity in the two families ; secondly, that it is not due to the commingling of two germ plasms in one or both of which there is the undiscovered latent seeds of the neuropathic taint.

I have been able to obtain two pedigrees which I think will fulfil as nearly as possible these conditions. The first pedigree (Fig. 8) relates to a woman with two families ; by her first husband, with no history of the neuropathic taint in his family, she has healthy children and grandchildren, many of whom are grown up. She then married a man who was a drunkard, one of a family of drunkards, his father was a drunkard ; one of his brothers a drunkard had ten children, and of these one was deaf and dumb and another an imbecile, otherwise there was nothing in the family indicating an hereditary taint. The offspring of this woman by the second husband were as follows : a boy with pseudo muscular dystrophy ; a normal boy, and a feeble-minded epileptic imbecile. A glance at the pedigree seems undoubtably to show that the father's

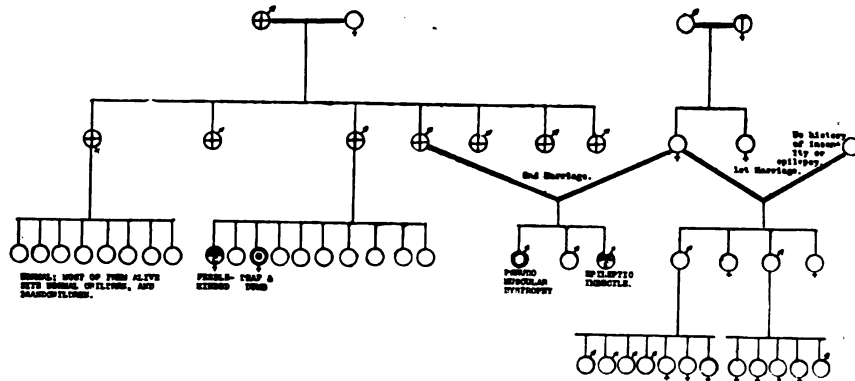


FIG. 8.

general germ plasm was accountable for these defects, and drink in successive generations the probable cause.

The next pedigree (Fig. 9) obtained for me by Mr. Leeming, is even more suggestive of alcohol and syphilis as a cause of epilepsy and insanity. Two brothers coming from a sound stock traced back two generations previously married two sisters. One sister died of alcoholic cirrhosis of the liver and paraplegia ; the other married twice. By her first husband she had children free from epilepsy and insanity, and by her second husband a child who had grandchildren, none of whom were affected. Her sister, who died of cirrhosis of liver and was a drunkard, was married to a man who very possibly had suffered with syphilis, as he died from the rupture of a large blood vessel (aneurism) ; there were nine living children, three were insane and one epileptic.

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The pedigree shows what happened to these, and this hereditary taint was transmitted to the next generation.

It may be a biological heresy, but it is firmly rooted in the minds of the majority of practising physicians that a chronic blood-poisoning (especially when occurring in successive generations) produced by the racial poisons, alcohol, syphilis and tuberculosis can *per se* cause degeneracy in a healthy

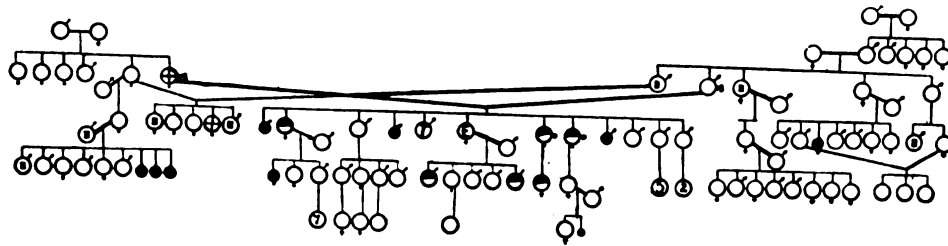


FIG. 9.—This pedigree is of interest in showing the marriage of two brothers with two sisters. In the first instance the male suffered with heart affection, which was transmitted to the offspring. In the second case the female suffered from cirrhosis of the liver and paraplegia, and was probably alcoholic and possibly syphilitic. The result was three insane and one epileptic offspring. From the first insane daughter the issue was apparently unaffected; but from the next daughter, who had masked epilepsy, of five children born two were insane. The next two insane daughters each gave birth to an illegitimate child by the same father; one of these children became insane at adolescence, whereas the other has married and has an apparently healthy child. H denotes heart affection. Half-black circles—insanity.

stock by a pathological mutation of the germ plasm which can be transmitted. Biologists say that you are assuming that an acquired character can be transmitted, and you must prove that the poison is not acting on the individual by reviving a latent neuropathic taint. In a great number of cases this is probably true, but a collection of pedigrees such as these two in a sufficient number would afford the proof required even by biologists.

The Investigation of Twenty-Five Pedigrees of Insane Persons.

By HILL WILSON WHITE, M.B., B.Ch., B.A.O.

Whilst I was in the service of the London County Council Asylums Committee, Dr. Mott suggested to me that I should endeavour to obtain some pedigrees, complete as far as possible, of insane persons.

In this article I propose to explain the method adopted in this research in the hope that it may prove of assistance to others interested in this matter, and to say a few words about each of the 25 pedigrees which I have obtained.

My first difficulty in this research was to find a method by which it would be possible to obtain all the information required concerning each member of the patient's relatives.

After some trials I hit on the method of using a separate book for each family tree. An extract from one of my books will help to explain this method.

The information was put in the form of 10 questions on two slips, five on each slip. These slips were pasted into the inside of the front and back covers of each book in such a way that when the book was opened the slips lay to the left side of the book, and as the pages of the book were turned over the top page lay to the right of the slip attached to the front cover and the bottom page lay to the right of the slip attached to the back cover. When the books were closed the slips were turned in, and to assist relatives in using the books a number of directions were printed on the back of the first slip.

In this way each of the 10 questions could be answered for each relative (or group of relatives) across each page of the book. On the first page of the book the word "Patient" was placed at the top of the page, and numbers corresponding were placed on the page opposite each question on the slips.

On the next page "Patient's brothers and sisters" was written at the top of the page, and columns were drawn down the page corresponding to the number of brothers and sisters. The answers for each question were to be

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	Patient's Father's Brothers and Sisters. Number 4.				
	Brother.	Sister.	Sister.	Patient's Father.	Brother.
1. Present Age. If dead state age at death and cause of death.	Died at 43. <i>Pneumonia.</i>	39.	37.	Particulars elsewhere.	34.
2. State whether the individual has ever had a mental breakdown or has ever been mentally defective. If so at what age and where treated.	Yes. When 22 years old. Treated at the Downs Asylum. Recovered after a year.	No.	No.		No.
3. State the nature of any complaints the individual has ever suffered from during life. Especially note eccentricity, hysteria, headaches, neuralgia, chorea or any nervous disease.	Measles when a child.	Measles and scarlatina. Bronchitis in later life.	Whooping cough, measles.		Always healthy.
4. State whether the individual is now or ever has been subject to— (a) Epilepsy. (b) Consumption.	No. No.	No. No.	No. No.		No. No.
5. General Health. State whether very robust, robust, normally healthy, rather delicate, delicate or very delicate.	Normally healthy.	Normally healthy.	Robust		Robust.

6. General Ability.	(a) State at what kind of school the individual was educated—private school, board school, truant school or "special school."	Board School.	Ditto.	Ditto.	Ditto.
	(b) Standard reached at school.	Sixth.	Sixth.	Fifth.	Fifth.
	(c) General Intelligence and Business Capacity.	Above the average.	A clever housewife.	Average.	A very clever mechanical engineer.
7. Temperament.	Sanguine or melancholy or an unstable combination of both.	Sang.	Sang.	Sang.	Sang.
8. Alcohol.	State whether the individual has been an abstainer, a moderate drinker, periodic abuse or constant abuse.	Moderate.	Abstainer.	Moderate.	Periodic abuse.
9. Note whether the individual has ever been in prison ; if so, for what reason.		No.	No.	No.	No.
10. In case of mothers of any relatives, state number of children, noting order of births. In case of brothers and sisters of any relatives state number of children, noting order of births. In these cases state whether the other parent (father or mother) was healthy and mentally sound. In all cases state whether the children are healthy and mentally sound. Note any miscarriages or difficult labours.		Four. Boy, boy, boy, girl. Children and their mother healthy and mentally sound.	Two. Boy, girl. Children and father healthy and mentally sound.	Three. Boy, girl (epileptic), girl. Father and all children except second (girl) healthy and mentally sound. Second girl epileptic.	Not married.

placed opposite the corresponding numbers as on the previous page. The same method was adopted for the patient's father, father's brothers and sisters, &c., up to the patient's great-grand-parents on each side—paternal and maternal.

In order to assist relatives in filling in the book, I placed a "specimen page" with answers filled in at the end of each book. One of these specimen pages is shown in the table. That this method was not difficult to understand is shown by the way in which most of the patients' relatives to whom I wrote were able to fill in the books.

The books used were ordinary scribbling books, $8\frac{1}{2}$ by $3\frac{1}{2}$ inches.

The following is the list of questions, which are based on those formulated by Dr. Mott, and used by him in constructing pedigrees :—

1. Present age.

If dead, state age at death and cause of death.

2. State whether the individual has ever had a mental breakdown or has ever been mentally defective.

If so at what age and where treated.

3. State the nature of any complaints the individual has ever suffered from during life.

Especially note eccentricity, hysteria, headaches, neuralgia, chorea or any nervous disease.

4. State whether the individual is now or ever has been subject to :—

(a) Epilepsy.

(b) Consumption.

5. General health.

State whether very robust, robust, normally healthy, rather delicate, delicate or very delicate.

6. General ability.

(a) State at what kind of school the individual was educated—private school, board school, truant school or "special" school.

(b) Standard reached at school.

(c) General intelligence and business capacity.

7. Temperament.

Sanguine or melancholy or an unstable combination of both.

8. Alcohol.

State whether the individual has been an abstainer, a moderate drinker, periodic abuse or constant abuse.

9. Note whether the individual has ever been in prison ; if so, for what reason.

10. In case of mothers of any relatives, state number of children, noting order of births.

In case of brothers and sisters of any relatives, state number of children, noting order of births. In these cases state whether the other parent (father or mother) was healthy and mentally sound.

In all cases state whether the children are healthy and mentally sound.

Note any miscarriages or difficult labours.

Little remark is needed in regard to the questions themselves except, perhaps, to meet a possible criticism, namely, "Why is there no mention of syphilis or venereal disorders?" The reasons for omitting these questions were that (1) in many cases the relatives could not reply; (2) in more cases they would not tell; (3) the fact of being asked such questions would prevent many from giving any replies at all; (4) the possibility of judging from the history of miscarriages, &c. Indeed, some of the replies to question No. 9 as regards prison confirm me in the opinion as to the wisdom of omitting syphilis in the list of queries.

Now as regards the difficulties met with in this inquiry after the initial one of method.

The books were sent out to the relatives, and as each one was returned it was gone through carefully and a list made of any omissions in the replies.

These were made up in the form of a further series of questions (in some cases occupying another book) and sent back to the relatives. In some cases this process had to be repeated two or three times. In other cases it was possible to obtain an interview with a relative and so to clear up ambiguities more quickly.

If there was any reference to a patient in another asylum an inquiry was made from the superintendent of such asylum.

It is interesting to note how much further information was obtained in many cases by following up clues, and by hammering away at the same questions until satisfactory replies were received. What the relatives thought of it is quite another matter!

Another difficulty met with was the fact that in some cases the relatives did not reply at all, and in other cases they had not sufficient information to form the basis of a pedigree.

The 25 pedigrees published are the result of 40 attempts to obtain information.

It is, in truth, obvious that anyone who takes up such an inquiry will be sure to meet with many failures in obtaining information.

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Before proceeding to the individual pedigrees, I would like to state that in choosing patients for this research I made no attempt to choose those who showed from the Asylum records that a "good insane stock" was to be expected.

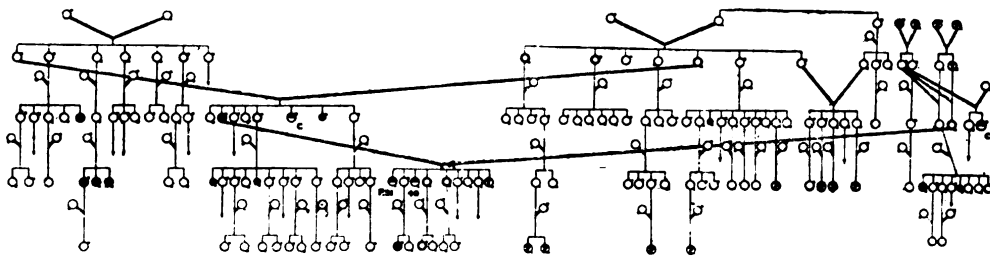
The only point laid stress on was to choose, whenever possible, patients who had one or both parents living, as in those cases I might expect to be able to trace the family tree back with certainty to the grand-parents, and in many cases to the great-grand-parents. No other point was thought of in choosing the patients.

I propose now to say a few words about each of the 25 pedigrees.

The following symbols, introduced by Dr. Mott, are used in the pedigree charts :—

○ = NORMAL.	◐ = INSANE.
⊙ = PARTICULARS UNKNOWN.	⊕ = INSANE AND ALCOHOLIC.
⊗ = BRILLIANT.	Ⓔ = EPILEPTIC.
Ⓐ = TOTAL ABSTAINER.	○ = NERVOUS DISEASE.
⊕ = ALCOHOLIC.	Ⓢ = SUICIDE.
Ⓓ = CONSUMPTION.	⊗ = "PECULIAR."
● = DIED YOUNG.	ⓧ = WANDERED AWAY.
⦿ = MISCARRIAGE.	

PEDIGREE No. I.



Obtained from patient's father and paternal uncle. This is one of the most remarkably complete and interesting pedigrees I have obtained. The patient is a female, aged 51 on first attack. Mental disorder—chronic melancholia. She is at times subject to well-marked delusions of persecution. There is a history of "severe epileptic fits when about four or five months old and

subsequently in infancy—with occasional attacks in after life.” At school age “she was hardly equal to other girls in practical everyday life. A certain degree of eccentricity” was noted. Not married. No children. Patient has a sister who became insane at 40 years old. She, like the patient, has well marked delusions of persecution, and was at one time in prison for 14 days “for contempt of court by non-appearance on summons for assault under alleged great provocation.”

She is the only example in all my family histories of a patient who is admitted to have had a relative in prison!

The sister who was imprisoned has history of a single attack of “epileptic fits” when under 12 months old. There was no recurrence of this attack.

One of the patient’s nephews (now 12 years old and healthy) is stated to have suffered from meningitis when an infant, with screaming fits at night. These attacks continued for some years.

On the paternal side we have four cases of mental brilliancy. The patient’s father, who supplied me with most of this very complete history, is mentally well above the average—a modern language and classical scholar. Three of the patient’s second cousins on this side are authors, one being very well known indeed to the reading public.

One of the patient’s father’s brothers was mentally deficient—“eccentric and *not* of business capacity throughout life.” The patient’s father’s mother suffered from “severe neuralgia in middle life.” On her side is seen a marriage of first cousins with no apparent harmful result as far as the subsequent history can be obtained. Otherwise the paternal side, which has been very fully traced for five generations, shows normal individuals. There are a fair number of the family who have been subject to headaches, which have been of sufficient severity to be remarked in the family history in answer to question No. 3.

On the maternal side there are some points of interest. Patient’s mother, who appears to have been always normal mentally, died from cerebral hæmorrhage at the age of 38. Her father, as will be seen from the pedigree, married three times. By his first wife he had a daughter who married and had eight children; the first of fair mental power and an authoress, and the last an epileptic. By his second wife—the sister of his first wife—he had a daughter, patient’s mother. By his third wife, no relative of the first two, he had a healthy daughter and a son, who was mentally deficient.

Although I made the fullest inquiries possible I was unable to find out any particulars of the patient’s maternal great-grand-parents. This was a great pity, as this man was by his three marriages the father of three healthy daughters (one who died of cerebral hæmorrhage) and a mentally deficient

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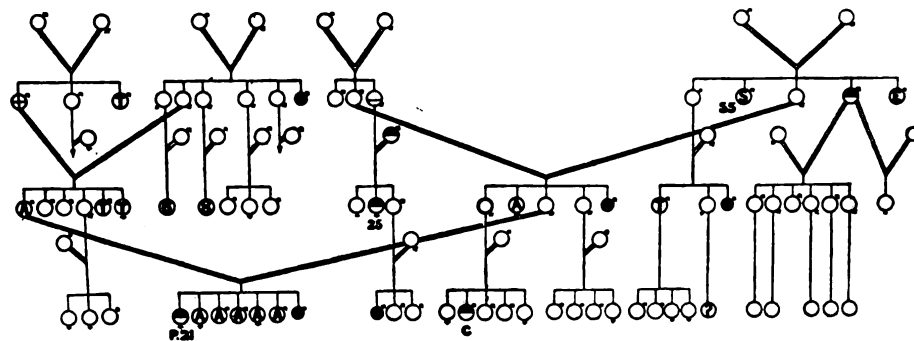
son—was the grandfather of two insane, one epileptic, and one mentally brilliant person, and thirteen normal persons—and was the great-grandfather of one child who was subject to “ epileptic ” fits for the first few years of life and of *over* eight who are normal up to the present time. Thus the stock which has been carried on has been the normal, not the abnormal.

As will be easily counted in the family tree, we have over 220 individuals about whom information has been given.

Of these we have two insane (both after 40 years of age), two mentally deficient, one epileptic throughout life, one who suffered from severe neuralgia in middle life, one from night terrors during first few years of life, one from cerebral hæmorrhage, and five who were brilliant mentally.

So that we have 215 who were not insane nor epileptic, many of whom brought up large and healthy families, and five of whom were mentally brilliant, and four insane and one epileptic, none of whom married, and who therefore did not carry on their abnormalities.

PEDIGREE No. II.



Obtained from patient's father. A very interesting pedigree showing melancholic temperament, suicide, insanity and neuropathy on maternal side. Female, aged 21 on first mental breakdown—primary dementia. Patient's brothers and sisters are all stated to be of the sanguine temperament and are normally healthy. The paternal side, of sanguine temperament, appears normal save for patient's father's father who took to drink late in life and died of apoplexy.

On the maternal side we have patient's mother's eldest sister who was hysterical and melancholy in disposition. She had, by a healthy husband, four healthy children and one child congenitally mentally deficient. Patient's mother's second sister, unmarried, was excitable and melancholy in disposition. Patient's mother, who suffered from headaches, was melancholy in temperament, and her next sister was excitable and melancholy in temperament.

Patient's mother's father suffered from headaches and was of melancholy temperament. His sister, of a similar disposition, married a man who afterwards died from "softening of the brain." They had two healthy children and one who became insane (periodic insanity) at the age of 25.

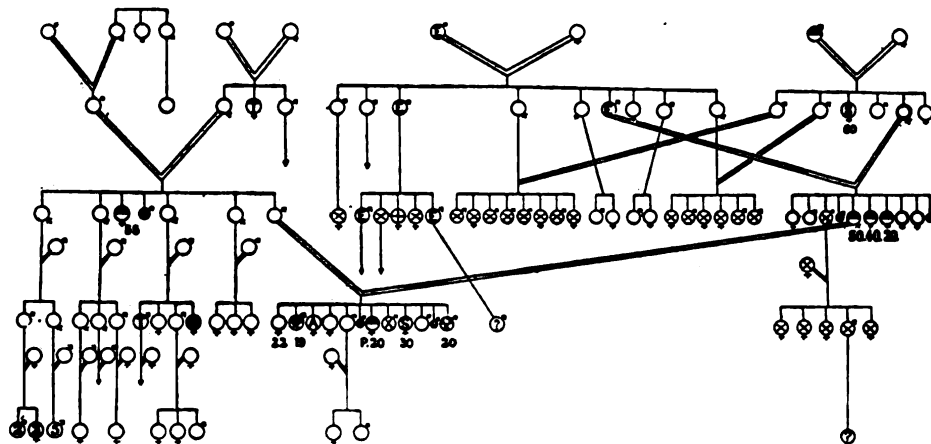
Patient's mother's mother was "excitable, nervous, and melancholy." Her second brother, unmarried, committed suicide by poisoning himself at the age of 55. Another brother with healthy children and grandchildren suffered from periodic insanity. Age at onset unknown. Another brother, unmarried, was epileptic from birth.

This pedigree is interesting, and the following points may be noticed in it :—

1. The marked melancholic temperament on the maternal side, which in one case resulted in suicide.
2. The evidence the pedigree gives of the way nature eliminates the unfit elements even in a very neurotic stock—by the fact that in the younger generations the insanity shows itself as congenital, or in early life, before marriage has taken place.

This fact has been noted before and will be seen in most of the pedigrees published here.

PEDIGREE No. III.



Obtained from patient's father. This is one of the most complete and interesting pedigrees which I have obtained.

Female, aged 31 on mental breakdown—manic-depressive insanity.

The details of interest concerning the relatives in this pedigree may best be described in order. Patient's brothers and sisters were as follows :—

1. Brother. Died at 37 years old. For 15 years had suffered from disseminated sclerosis.

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2. Brother. Had mental breakdown at 19 and again at 23. He was found dead by exposure at the age of 25, having wandered away from home.
3. Sister. Normal.
4. Sister. Normal.
5. Brother. Normal. Married with two healthy children.
6. Brother. Died at 11 months (convulsions).
7. The patient.
8. Brother who was found dead at 30 years of age, having wandered away from home.
9. Sister. Committed suicide at 30 years old.
10. Brother. Normal.
11. Brother. Died at 3 years old (convulsions).
12. Brother. Insane (melancholia) at 20 years of age. Committed suicide at 22.

It will be noticed that only one of this family of 12 married.

On the paternal side we have patient's father, who supplied me with the family history. He is quite above the average in intelligence, very temperate and sanguine in disposition. One of his sisters became insane between 55 and 60. She recovered and had no recurrence of mental disorder, dying at 81 years of age. All the remaining members of the paternal stock, as shown in the pedigree chart, were normal individuals. Many of them were married and have had healthy children and grandchildren.

On the maternal side of the family we see three marriages in two families—two daughters and one son, A, B, C, of an epileptic father (patient's mother's father's father), marry two sons and one daughter, A, B, C, of an insane father (patient's mother's mother's father). In *every* case the resulting offspring are mentally abnormal.

Patient's mother is hysterical and depressed ; of melancholic temperament. At the age of 50 became insane—exciting cause being death of her eldest son. She has never completely recovered.

Patient's mother's brothers and sisters are as follows :—

1. Sister. Hysterical and of melancholic temperament.
2. Brother. Eccentric and peculiar ; of melancholic temperament.
3. Brother. Rather peculiar in manner and of sanguine temperament. His wife is described as mentally sound "but very peculiar." They had five children, who are all described as "very peculiar." One of them married and has four children.
4. Brother. Died in infancy (convulsions).
5. Patient's mother.
6. Sister of melancholic temperament who became insane at 40.

7. Sister of melancholic temperament, who became insane at 20 and remained so until her death at 58.
8. Sister of melancholic temperament, and who suffered from nervous headaches.
9. Sister of "very sanguine" temperament. She also suffered from severe headaches.
10. Brother. Died in infancy.

Patient's mother's father was an epileptic. His brothers and sisters were as follows :—

1. Brother, who died at 48 years old of a "fit." It is not known whether he was an epileptic. He had one daughter, who is described as sound mentally, but "very peculiar."
2. Sister. Normal. Married. No children.
3. Brother, of melancholic temperament and epileptic all his life. He married and had five children who are described as follows :—
 - (a) Son, epileptic. Married, no children.
 - (b) Daughter, married. No children. A very peculiar woman and said to be addicted to drink.
 - (c) Daughter, unmarried, rather peculiar in manner, but kind hearted, and what the world would call "sharp."
 - (d) Daughter, unmarried, "half idiotic," dead.
 - (e) Son. Subject to epileptic fits. Has one son about whom further particulars are unknown.
4. Sister. Normal. Married one of patient's mother's mother's brothers and had eight children, who are described as "peculiar," and have not done well in life.
5. Sister. Normal. Married with two children.
6. Patient's mother's father.
7. Sister. Normal. Married. No children.
8. Brother. Normal. Married. Two children.
9. Sister, normal, who married one of patient's mother's mother's brothers and had six children, who are described as "peculiar." None of them did well in after life.

Patient's mother's father's father was an epileptic nearly all his life. Patient's mother's mother was of melancholic temperament and subject to severe headaches. Her brothers and sisters were as follows :—

1. Brother, normal, who married patient's mother's father's sister. (4 above.)
2. Brother. Normal. Married patient's mother's father's sister. (9 above.)

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3. Sister of melancholic temperament. Unmarried. Addicted to drink in early life, and committed suicide at 60 years of age.
4. Brother. Died young.
5. Patient's mother's mother.
6. Sister. Normal. Unmarried.

Patient's mother's mother's father is stated to have died in an asylum when about 35 years old. In reviewing this very full pedigree one may note the following points :—

1. As to temperament—that of the healthy members and that of many of the unhealthy members of the stock is sanguine. The exceptions are seen from the letterpress.
2. The three marriages on the maternal side are very interesting and instructive.

One sees in the best traced out of these marriages, namely, that of patient's mother's father and patient's mother's mother—that *all* the offspring are very abnormal ; and in the further tracing out of the pedigree one sees the family almost disappear—through insanity, suicide, and non-marriage. As to the other two marriages one knows that all the resulting offspring were “ peculiar.” Owing to family divisions and separations it has not been possible to trace these two families out as fully as that of patient's mother's mother.

But looking at the whole maternal stock, and judging from the members whom we have been able to trace fully, one sees how Nature finally wipes out the unfit elements in a few generations.

PEDIGREE No. IV.

A very complete pedigree of five generations, obtained from patient's mother, showing insane heredity on both sides.

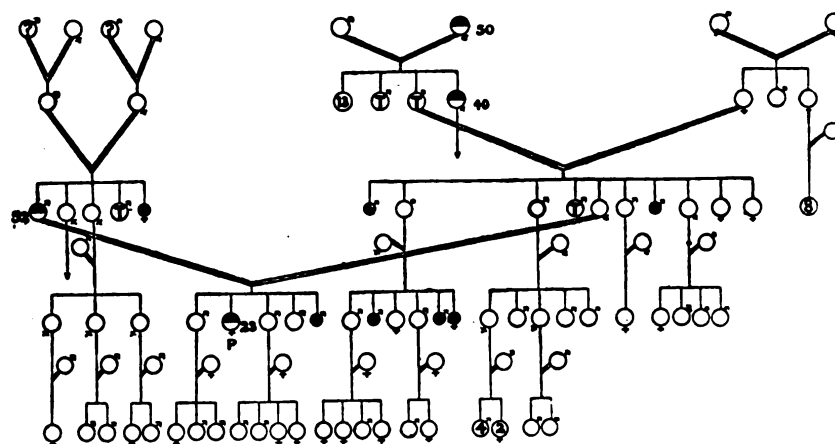
Female, aged 38 on second attack. Previous attack at age of 23, from which she recovered in two years. Mental disorder—melancholia. On the paternal side we notice that patient's father died at age of 52 from “ acute melancholia followed by inanition,” according to the death certificate. His mental disorder is stated to have been brought about by business worries and the illness of his daughter.

One of his brothers was a consumptive and occasionally exceeded in alcohol. Otherwise the paternal side was healthy as far as could be traced.

On the maternal side we remark that one of patient's mother's brothers was consumptive, another asthmatic.

Patient's mother's father died of consumption. He was one of 16 children, one of whom also was consumptive. The youngest of this family, a daughter,

became insane at 40 years old. She recovered from this attack. She was married, but had no children. Patient's mother states that there was a remarkable similarity in disposition between this individual and her daughter (the patient), that her daughter "took after" her in a marked manner. Patient's mother's father's mother became insane at 50 years. The attack lasted three years with recovery, and she had no further attack before her death at age of 58.



In regard to this pedigree there are two points of much interest to be remarked—firstly, the ages of onset of insanity in the various individuals should be noted with regard to the occurrence of "anticipation"; secondly, it should be noted how many healthy individuals have sprung from a moderately bad stock, and how the abnormal has not succeeded in carrying itself on beyond a few generations.

PEDIGREE No. V.

Obtained from patient's mother. Female, aged 19 on mental breakdown (juvenile general paralysis). Patient's brothers and sisters may best be described in order as they show a typical syphilitic family.

1. Brother. Died of convulsions 1½ days.
2. Brother. Died of convulsions 24 days.
3. Miscarriage.
4. Brother. Died of intussusception at one month.
5. Brother. Died of convulsions at one month.
6. Brother, now aged 24. Married, with two children. Was subject to fits until five years old and to neuralgia at about fourteen years. Now suffers from violent headaches.
7. The patient.

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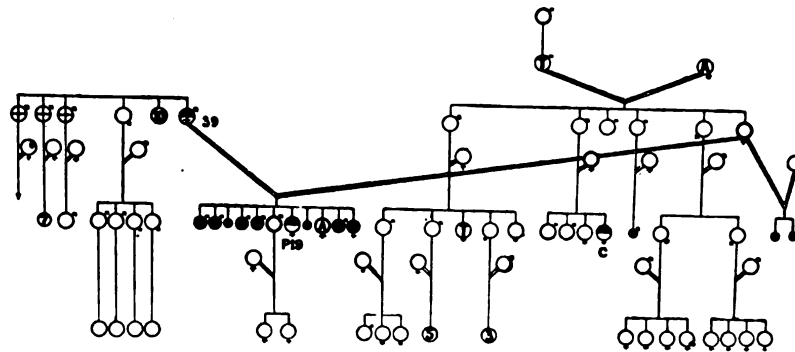
8. Miscarriage.

9. Sister, now aged 19. Suffers from severe headaches and is "peculiar at times."

10. Brother. Died at one year—(diphtheria).

11. Sister. Died at four years—(blood poisoning).

After patient's father's death from general paralysis, patient's mother married again and had two miscarriages (three months and seven weeks), with no further pregnancies. Her second husband is healthy. On the paternal



side we have patient's father who died in Cane Hill Asylum from general paralysis at age of 41. Disease commenced two years before. Patient's father was the last of 15 children. The eldest three brothers about whom we have particulars were all heavy drinkers.

On the maternal side we have patient's mother, who suffered from severe headaches. Her brother and sister were healthy. Her second brother married a woman who at the age of 47 became "queer" and "deaf, with an impediment in her speech." They had three healthy children, and one who was congenitally mentally deficient.

Patient's mother's father's father suffered from paralysis agitans.

PEDIGREE No. VI.

Obtained from patient's mother and uncle. A remarkably full pedigree, which shows insane heredity on both paternal and maternal side, and which is of great interest from the number of cases of suicide or insanity which occur about the age of 43.

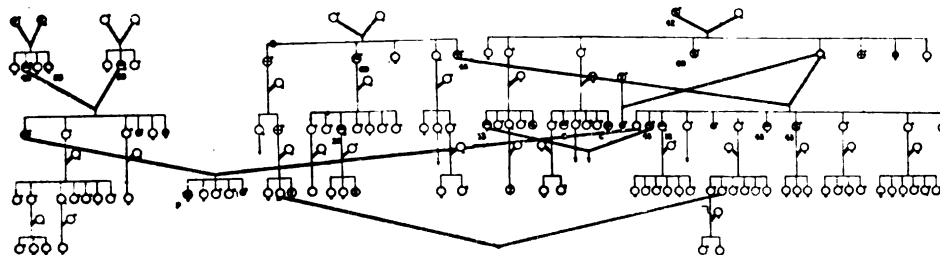
Female, aged 33 at present. Has always been mentally deficient (congenital mental deficiency). She and her sister and brothers are unmarried.

Paternal side.—Patient's father and his brothers and sisters and their offspring were healthy. Patient's father's father became insane at 48, but recovered after a year. There was no recurrence of insanity before his death at age of 77. His youngest sister was paralysed from the age of 35, but

mentally sound. She lived until the age of 80. His two other sisters had several healthy children. No information could be obtained concerning his parents. Patient's father's mother became insane at 80, and remained so until her death at 85 (senile dementia). She had a sister who was unmarried, and a brother about whom particulars were unknown. Her parents were mentally sound.

Maternal side.—Patient's mother has suffered from neuralgia, which commenced at age of 18, and is hysterical. Her eldest brother committed suicide at age of 43 by hanging. He married his first cousin, who became insane at 43 with recovery after some time, and he is stated to have committed suicide as a result of grief at her insanity.

Patient's mother's eldest sister had "temporary religious depression" at age of 18 years. She married and had six healthy children, none of whom married. Another of patient's mother's sisters became insane at age of 43 and remains in an asylum. The next brother committed suicide by drowning at age of 43—his suicide being stated to have been brought about by sudden mental stress and influenza. He had three healthy daughters, none of whom married.



Patient's mother's father became insane at age of 43—insanity stated to be due to financial troubles. He was in an asylum for six months, recovered, and had no further attack; he died aged 69.

His eldest brother was intemperate at times, and had a healthy daughter and a son who was a drunkard.

His second brother became insane at about 60 years old, and remained so until his death a short time after. He had six healthy children, and a daughter who became insane twice after childbirth, at 20 and at 22 years of age. Each attack lasted six months, and resulted in recovery. The members of this family went to Canada when young, but were mostly married, and had healthy offspring.

Patient's mother's mother is stated (by patient's mother) to have been a great sufferer from neuralgia. She married twice, and her first husband died of consumption at 40 years of age, leaving one child, who died in infancy.

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Particulars as to her second husband (patient's mother's father) and offspring have already been given.

Her eldest brother married and had seven healthy children, and one daughter who became insane at 43. She, as stated before, married her first cousin (the eldest brother of patient's mother), who committed suicide at 43.

Patient's mother's mother's next brother married his second cousin, who is described as having been "odd tempered" and "somewhat feeble-minded." They had four healthy children, and a son and daughter who were both mentally deficient. Patient's mother's mother's next brother went to Australia and made money. He returned to England and started farming, at which he failed. He committed suicide at age of 60 by taking poison. He was unmarried.

Patient's mother's mother's next brother was a drunkard. Patient's mother's mother's father committed suicide at age of 42 by hanging himself. This act was stated to have been occasioned by mental strain arising out of business difficulties.

The points of interest to be noted in this pedigree especially are :—

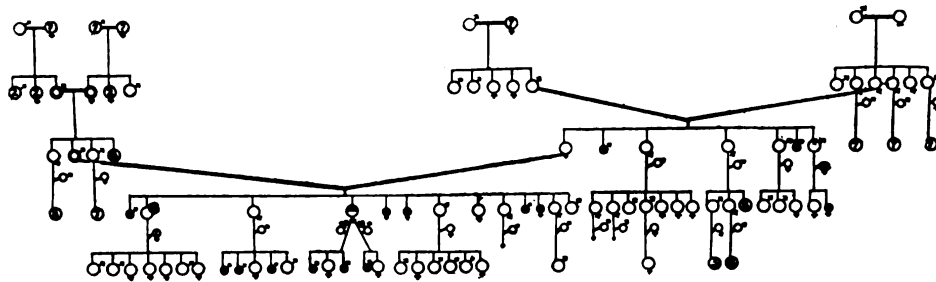
1. On the paternal side the large number of healthy descendants of patient's father's father and patient's father's mother, both of whom became insane.
2. On the maternal side the ages of onset of insanity or of suicide. These should be noted in relation to "anticipation."

Thus we have patient's mother's mother's father committing suicide at age of 42. One of his sons committed suicide at 60. Two of his granddaughters became insane at 43, two of his grandsons committed suicide at 43, one of his granddaughters had "temporary religious depression" at 18, and another granddaughter (patient's mother) began to be a sufferer from severe neuralgia at 18. A grandson and a granddaughter were mentally deficient from birth. The same was true of his great-granddaughter, the patient. One can see that the ages of onset of insanity gradually decrease as one traces down the pedigree—the same decrease is not noticed in the case of those who committed suicide.

PEDIGREE No. VII.

Obtained from patient's sister. Female aged 35 on admission to asylum. Probably a case of traumatic epilepsy.

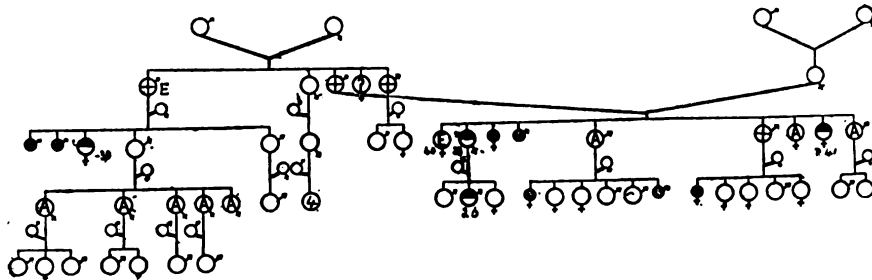
There is a history of fits from 6 to 21 years, due to a fall, and of a maniacal attack at 18 years which was treated at home. Also a similar attack at age of 34. Patient while in asylum had recurrent maniacal attacks, but no fits. She was discharged recovered in a year.



This is a fairly complete pedigree of five generations showing no insane relative. There is a history of asthma in case of patient's father and his parents.

In this case there is no insane heredity ; the maniacal attacks were probably epileptic equivalents, and the epilepsy was traumatic in origin.

PEDIGREE NO. VIII.



Supplied by patient's nephew.

A full pedigree of five generations showing bad temper, drink and insanity on paternal side of stock.

Female aged 41 on admission to asylum in 1911. Previous attack in 1902 with recovery in 14 months. Recurrent melancholia with recovery.

Patient's eldest sister, unmarried, became epileptic at 40 years of age. Her second sister became insane (chronic mania) at 38, and died in an asylum 10 years later. She had three children by a consumptive husband. Her second child became insane at 26 years old (dementia præcox), and died in an asylum. Remaining two children healthy (unmarried).

Patient also had three brothers, married with healthy offspring, and one sister unmarried. Patient's father and his two brothers "were all men of violent bad temper, sometimes when sober, sometimes when in drink." The

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eldest brother became epileptic at 30 years of age. His daughter, unmarried, "was driven out of her mind (before 30 years old) by her father's continual cruelty and violent bad temper, which put her in such fear and terror that it sent her out of her mind." Both her brothers were healthy and had healthy offspring.

Patient's paternal grandparents were healthy, and there appears to be no heredity taint on the maternal side.

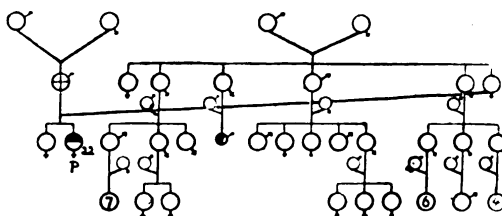
This pedigree is interesting, as it shows how Nature can weed out the bad elements of a stock.

Thus we see that patient's father, a drunkard, had :—

1. A daughter (epileptic), unmarried.
2. A daughter (insane), married, with two healthy children, unmarried, and a son, who had dementia præcox.
3. The patient, unmarried.
4. Three sons, one a drunkard, two total abstainers, married, with healthy offspring, and an unmarried daughter.

Patient's father's brother, an epileptic, had one insane daughter unmarried, and two healthy sons with healthy offspring.

PEDIGREE No. IX.



Female, aged 39 on admission to an asylum for second time (was in an asylum for six months when 22).

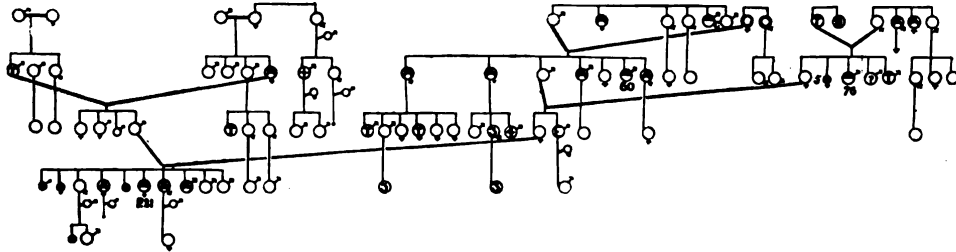
Mental disorder (secondary dementia).

This is a short pedigree of four generations, obtained from patient's mother.

There is no evident heredity factor in this case, but it may be noted that it was not possible to obtain information of the past beyond patient's grandparents.

The only point of interest in this case is the large number of healthy individuals in the comparatively small stock.

PEDIGREE No. X.



A very complete pedigree, obtained from patient's mother, showing insanity on the maternal side.

Female (congenitally mentally deficient), sent to asylum at 21 years old. The paternal side, which has been very fully traced out for five generations, is normal mentally. There are a few cases of consumption, which disease has not been carried on into the younger generations.

On the maternal side we have patient's mother's brother, who is stated to have had two "epileptic" fits at 24 years of age with no recurrence.

One of patient's mother's father's brothers died at 69 through drinking—he was certified as "insane" before his death. One of patient's mother's father's father's brothers was congenitally mentally deficient, and patient's mother's father's mother and her sister suffered from true asthma. One of patient's mother's mother's brothers suffered from neuritis, and became insane at 76 years of age (senile dementia).

This pedigree is of interest from the large healthy paternal stock, and in showing the large number of healthy individuals on the maternal side. It may also be noted that none of the members of the stock who became insane have produced offspring.

The temperament of the members of this stock is described on both paternal and maternal sides as sanguine save for four individuals on the maternal side, namely, patient's mother's father's father and his brother, patient's mother's father's mother's sister, and patient's mother's mother's brother.

PEDIGREE No. XI.

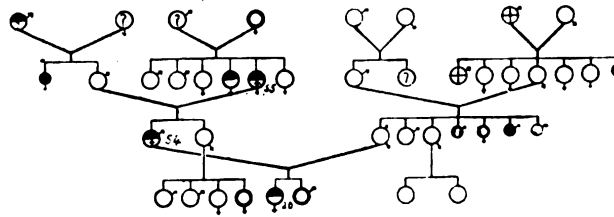
Supplied by patient's mother. Pedigree shows well-marked eccentricity, hysteria, alcoholism and insanity on the paternal side.

Female, aged 28 on second attack. Previously in asylum for five years, at age of 20. Recurrent melancholia.

Patient's brother is neurotic, hysterical, and at times subject to fits of depression.

Patient's father was eccentric, hysterical, and at times exceeded in alcohol. He died at 54 years of age, having had a complete mental breakdown three

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weeks before his death. He and his sister are described as having been of melancholic temperament; she has four children—the last was hysterical and slightly eccentric.

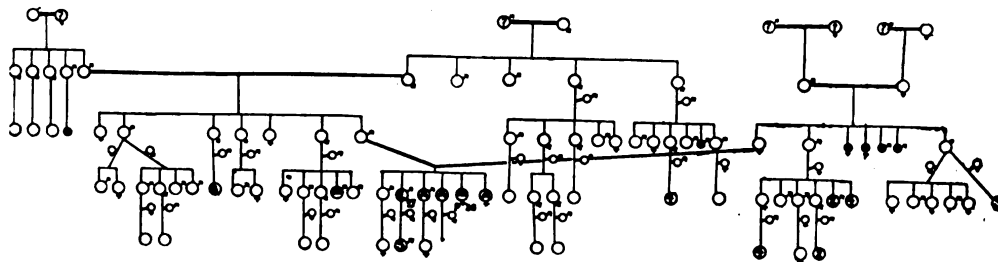
Patient's mother states that she *thinks* patient's father's father's father was in an asylum at one time.

Patient's father's mother was eccentric and very hysterical all her life. She was a continuous secret drinker, and had a mental breakdown some time when between 50 and 60 years of age. Died when 75. Patient's father's mother had one sister who was insane—age at onset of insanity unknown.

Patient's father's mother's mother was very hysterical and occasionally exceeded in alcohol.

The maternal side shows normal individuals save for two alcoholics.

PEDIGREE No. XII.

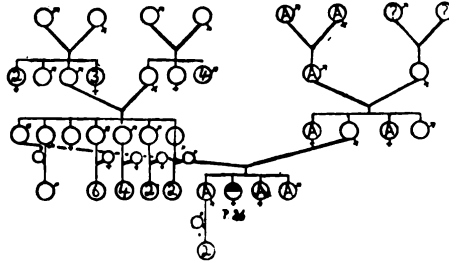


Obtained from patient's father. This pedigree shows dementia præcox occurring in a remarkably large and healthy stock.

Female, aged 26 on mental breakdown (dementia præcox). Patient is one of six children. All the others are healthy save one brother, who has been epileptic since 17 years of age.

On the paternal side we have a very large, fully traced-out stock, healthy with two exceptions—patient's father's father asthmatic and a son of one of patient's father's sisters who is insane—the age at onset of insanity being unknown. On the maternal side again is seen a large healthy stock with one exception, patient's mother's father, who was asthmatic.

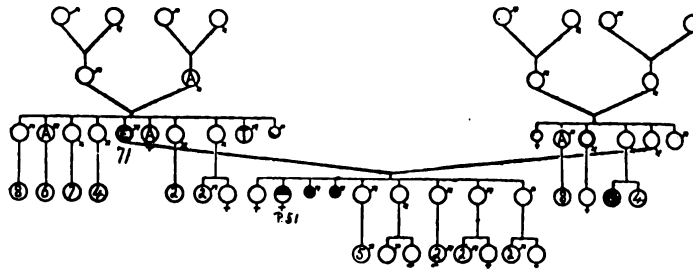
PEDIGREE No. XIII.



Obtained from patient's father. Female, aged 26 on mental breakdown (chronic mania).

This pedigree calls for little comment. As far as can be ascertained there appears to be no neurotic taint on either paternal or maternal side.

PEDIGREE No. XIV.



Obtained from patient's sister and parents. Female, aged 51 on mental breakdown (melancholia). Patient's father suffers from senile epilepsy, which commenced at 71 years of age.

One of patient's mother's sisters suffered from sciatica, which commenced between 40 and 50 years of age. As will be seen from the pedigree chart there are no other neuroses. Patient comes from a very long lived and healthy stock on both sides. There is one case of consumption on the paternal side (father's brother), and two of patient's mother's sisters died in middle life from the same disease. Otherwise the stock is remarkably healthy.

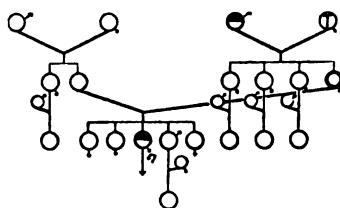
PEDIGREE No. XV.

Obtained from patient's sister. Female, aged 57 on mental breakdown (recent melancholia). Patient was always rather delicate and suffered from nervous debility. The present attack was brought on by ill-health and family troubles. Patient had three sisters (unmarried), and a brother who had six or seven normal children. Patient's father died of apoplexy when aged 83. His parents were healthy.

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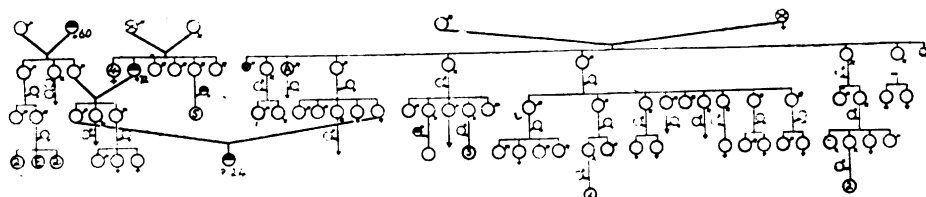
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Patient's mother was a neuropath—suffered from well-marked hysterical attacks. Her father died in an asylum. His insanity is stated to have been brought on by concussion—the age at onset of insanity unknown.

PEDIGREE No. XVI.



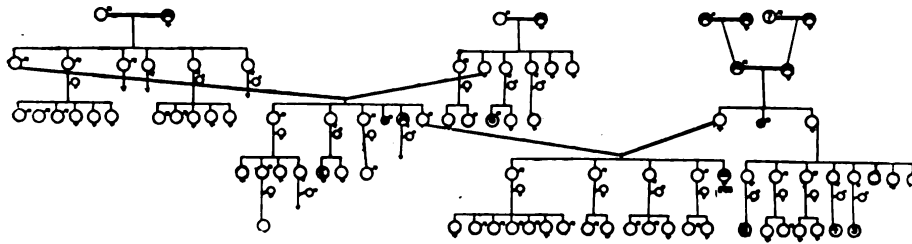
Supplied by patient's father. Female, aged 24 on mental breakdown (dementia præcox).

On the paternal side we have patient's father's father asthmatic, and a grandchild of one of patient's father's father's brothers an epileptic. Patient's father's father's mother was insane for a few months before her death at age of 60.

Patient's father's mother was insane for a short time at age of 72. One of her brothers married a woman who became twice insane after childbirth (puerperal insanity), with recovery. They had five healthy children. Patient's father's mother's father was noted as being eccentric. On the maternal side we have a very large healthy stock with some few exceptions. Patient's mother's father's third sister—not marked in pedigree chart as insane—became insane at the age of 68; she had healthy children, grandchildren and great-grandchildren as shown in the pedigree chart. Patient's mother's father's mother was eccentric in last three or four years of life. She died at the age of 84.

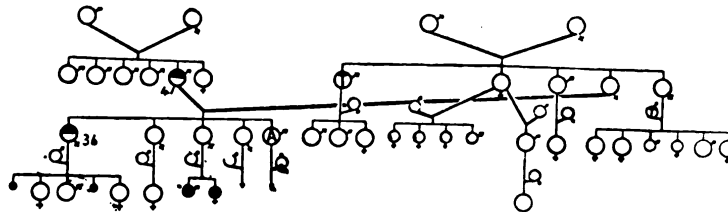
PEDIGREE No. XVII.

Obtained from patient's brother. Female, aged 33 on mental breakdown (dementia præcox). This is a very fully worked out pedigree and shows a large healthy stock, the only apparent exception being one of patient's first



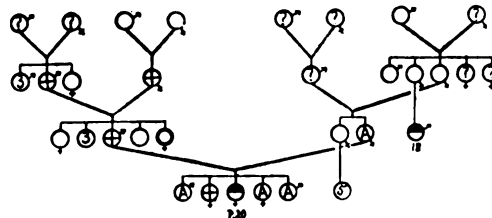
cousins (a daughter of patient's father's sister), who was subject to fits from birth.

PEDIGREE No. XVIII.



Supplied by patient's mother. Female, aged 36 on mental breakdown (melancholia). As will be seen from the pedigree chart the stock is a healthy one save for patient's father, who died of general paralysis at the age of 41.

PEDIGREE No. XIX.



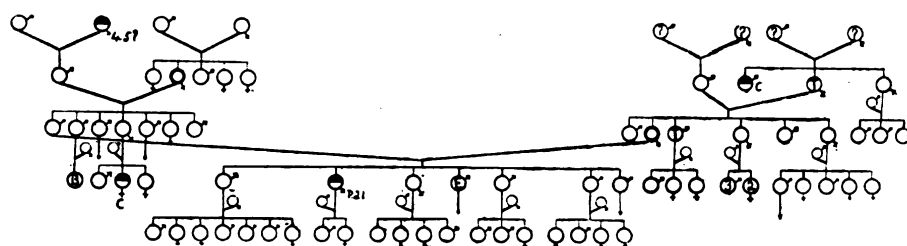
Supplied by patient's brother. Female, aged 20 on mental breakdown (mania). Patient has one brother who is occasionally alcoholic; her father was a well marked alcoholic for 16 years, and her paternal grandparents occasionally exceeded in alcohol. On the maternal side we have one of patient's mother's first cousins insane since 18 years old.

PEDIGREE No. XX.

Supplied by patient's father and brother. Female, aged 39 on mental breakdown (melancholia). She had a previous attack at the age of 21.

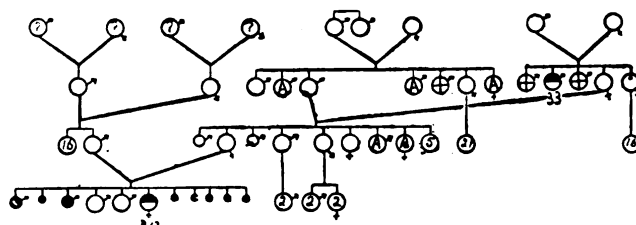
One of patient's brothers has suffered from epileptic fits up till two years ago. A first cousin (a daughter of one of patient's father's sisters) is an

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imbecile. Patient's father's father's mother died in an asylum, and patient's father's mother suffered from asthma. On the maternal side we have patient's mother an asthmatic and patient's mother's mother's brother an imbecile. The other members of the comparatively large stock are healthy.

PEDIGREE No. XXI.

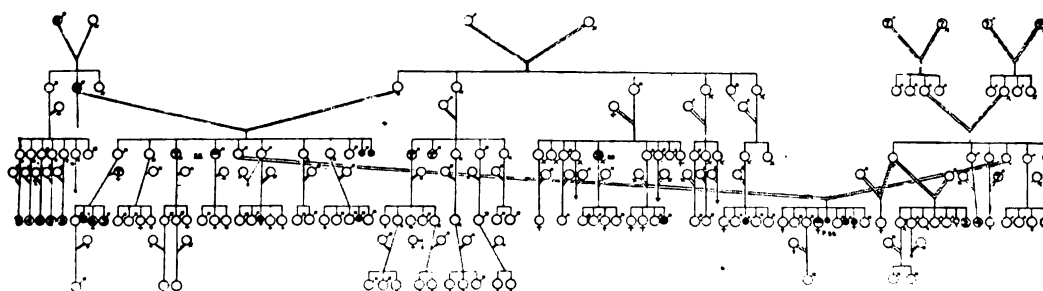


Obtained from patient's mother and mother's father. Female, aged 17 on mental breakdown (dementia præcox). One of the causes of patient's breakdown may have been exhaustion, patient's father being the last of 17 children and patient being sixth in the family, followed by five miscarriages.

Besides patient there is only one case of insanity in the stock, namely, patient's mother's mother's brother, who attempted suicide at age of 33 and was sent to an asylum.

The other members of the stock are normal, save for three alcoholics on the maternal side.

PEDIGREE No. XXII.



Obtained from patient's father, a working man employed "on the London Tramway Company and London County Council tramway for 20 years."

This pedigree comprises a great many individuals, and it must be pointed

out that all the questions have not been answered for each individual in this pedigree, except in the direct line of descent as far as was known. The main question as to sanity or insanity has been answered in each case, and as is seen from a glance at the chart the very large stock is on the whole a healthy one. This chart shows :—

1. What large capable families the working classes in this country can bring up.
2. And that it is possible to obtain a great deal of information useful to a student of heredity from the members of the working classes.

The patient's father, who gave me all the information in this case, is an uneducated working man, but the pedigree chart reflects credit on him from its completeness.

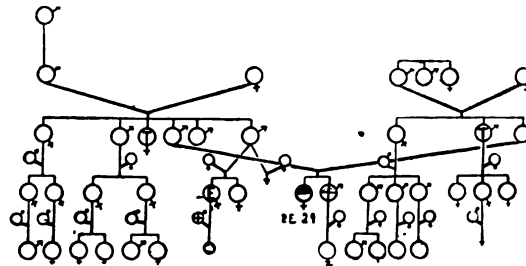
Female, aged 22 on mental breakdown (dementia præcox).

One of patient's father's brothers became insane at 35 years of age.

Patient's father's father was intemperate, and patient's father's father's father committed suicide (age unknown).

A daughter of one of patient's father's mother's brothers committed suicide at age of 35 (mind stated to have been deranged). The remaining members of the paternal stock and all the known members of the maternal stock, comprising a very large number of individuals, are seen to have been normal.

PEDIGREE No. XXIII.



Obtained from patient's father. Female, aged 29 on mental breakdown (insanity with epilepsy).

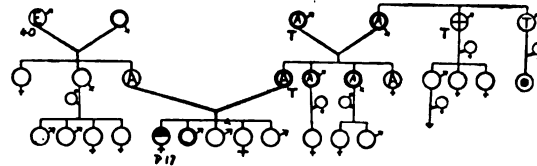
As will be seen from the pedigree chart the stock is small and made up from healthy individuals. No comment is required.

PEDIGREE No. XXIV.

Obtained from patient's parents. Female, aged 17 on mental breakdown (dementia præcox).

On the paternal side we have patient's father's father, who had epileptic fits at age of 40, and patient's father's mother who suffered from severe headaches.

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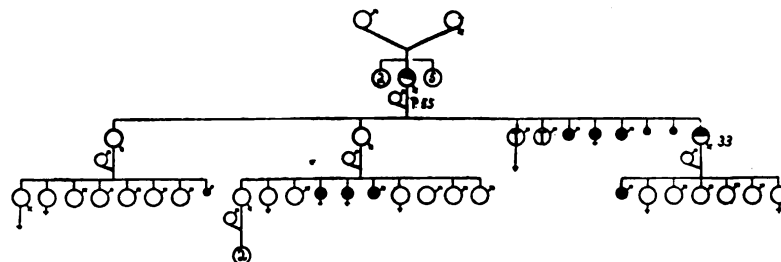


On the maternal side we find a neurotic stock. Patient's mother is hysterical and suffers from severe headaches. She had a severe hysterical attack lasting some months at the age of 36.

Patient's mother's brother suffered from severe headaches, and a sister was markedly hysterical and neurotic, and suffered from severe headaches.

Patient's mother's father and mother suffered from severe headaches, and patient's mother's mother's brother was an alcoholic and hysterical. Patient's mother's mother's second brother is stated to have been melancholic in temperament, the only one in the stock who is mentioned as having this temperament, all the others being cheerful or "very cheerful." He had 11 or 12 children who died in infancy. One may also note the occurrence of consumption on the maternal side. Thus patient's mother, patient's mother's father, and two of patient's mother's mother's brothers were consumptive. The disease does not occur in the younger generations.

PEDIGREE No. XXV.



Obtained from patient's daughter. Female, aged 55 on mental breakdown (dementia).

She had seven healthy children and one who became insane at 33 (delusional insanity). Her parents and grandparents were mentally sound.

Concluding remarks.

One may first notice the incidence of insanity in these 25 stocks. The following figures were obtained by counting up the number of *adults* in each paternal or maternal stock and the number of *adults* in each patient's own family, *i.e.*, the patient and his or her brothers and sisters. The individuals were grouped in each case as :—

1. Non insane or epileptic.
2. Insane.
3. Epileptic.

Paternal Stocks.

1. Non insane or epileptic	911
2. Insane	17
3. Epileptic	3

Maternal Stocks.

1. Non insane or epileptic	779
2. Insane	32
3. Epileptic	7

Patients' Families.

1. Non insane or epileptic	151
2. Insane	29
3. Epileptic	3
				<u>1,932</u>

This gives 78 insane persons among 1,932 individuals, or 40·37 per 1,000.

One may also notice the much higher proportion of insane in the maternal as compared with the paternal stocks. In regard to this one may note in passing that these 25 pedigrees are all of female patients.

"Anticipation."

Anticipation or ante dating by which "Nature tends to end or mend a degenerate stock" is shown in these pedigrees. In each pedigree chart the age of the individual at the onset of insanity is marked, and is seen to be in most cases smaller the further one descends in the pedigree.

As shown in the letterpress, the form of mental disorder in the younger generations is, in a great majority of the cases, of such a nature that it prevents the individual from propagating (adolescent insanity or congenital mental deficiency). In regard to this question one may infer (in these pedigrees at any rate), that in a given insane stock one can never tell where any individual will break down mentally, or whether he will break down at all. All one can conclude is that if an individual does break down he will do so, in all probability, at an earlier age than his parent or grandparent did.

Temperament in Insane Stocks.

In query No. 7, "Temperament—sanguine or melancholy, or an unstable combination of both," an attempt was made to obtain an idea of the trend of temperament in these insane stocks. I say "trend of temperament," for one knows how many different temperaments there are and how difficult it is to describe accurately the temperament of any individual, and how impossible it would be in an inquiry of this kind to obtain an accurate description of the

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temperament of each individual, even in the direct line of descent, in such extensive pedigrees as these.

Consumption.

Consumption occurs in 18 of the 25 pedigrees. In five of these 18 pedigrees only 1 case is recorded in the stock; in seven, 2 cases; in four, 4 cases; in one, 5 cases; and in one, 6 cases.

One may note in regard to these figures that in the case of certain numbers of the individuals the information was not forthcoming as to consumption—especially in the collateral branches of the families.

Looking over the cases where the information has been fully given, one finds that the disease occurs for the most part sporadically through the stocks, and there does not appear to be an inherited tendency to the disease.

Insanity and Epilepsy.

Excluding cases of insanity with epilepsy, 13 cases of epilepsy are recorded in the 25 stocks.

These cases occur in eight of the pedigrees as follows :—

In six pedigrees one case alone is recorded (Nos. 1, 2, 12, 14, 17, 20). Of these six epileptics two were married with healthy offspring; one (senile epilepsy) was married and had an insane daughter, six healthy children and 15 healthy grandchildren; one was married and had no offspring; and particulars as to the offspring of the remaining two were unobtainable.

In one pedigree (No. 8) two cases are recorded. One of these was the patient's sister (unmarried), and the other was the patient's father's brother, who was married and had two children who died young, an insane daughter (unmarried), and two sons with healthy offspring.

In one pedigree (No. 3) five cases are recorded—patient's mother's father's father, his two sons and grandsons. Full particulars have been given in the letterpress about his descendants. It may be noticed that no further case of epilepsy is recorded as one traces down the stock.

Suicide and Insanity.

Deaths by suicide are recorded in only four of the 25 pedigrees. All the cases, 10 in number, have been noted in the letterpress; this small number among so many individuals is interesting.

In conclusion I wish to express my gratitude to Dr. Mott for having proposed this most interesting study to me, and to thank him for his interest in the work and for the many suggestions he has given me.

I also wish to thank my former Medical Superintendents, Dr. Donaldson and Dr. Ogilvy, for permitting me to publish these records of patients under their care.

The Investigation of a Number of Family Histories of Patients in Cane Hill Asylum.

By J. C. WOORTON, M.R.C.S. Eng., L.R.C.P. Lond.

At Dr. F. W. Mott's suggestion, during the past year I have been carefully investigating the family histories of patients under my care at Cane Hill Asylum.

In a number of instances I have been able to obtain complete and accurate information regarding the stock for some generations back, and, as the complete pedigrees show many points of interest, I propose in this paper to describe these in detail.

Pedigree I illustrates the transmission of the artistic æsthetic temperament as shown by a high degree of musical and literary ability, &c., combined with very marked mental instability through five generations; complete histories have been obtained from both maternal and paternal stocks.

PEDIGREE I.

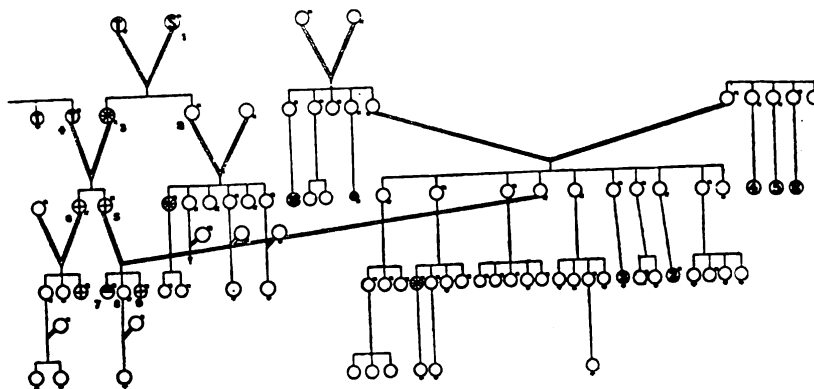


FIG. 1.—S. denotes *suicide*. Circles in octants—*genius*. Circles in quadrants—*alcoholism*. Half-black circle—*insanity*. Number inside circles denotes number of children; numbers outside circles are for reference in text.

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The pedigree commences with (1) a confirmed alcoholic and suicide. He was a sportsman, a collector of pictures, and was very extravagant; he committed suicide in a drunken frenzy. He married a woman who was always delicate, and who died early in life from tuberculosis. There were two children of this marriage.

The youngest (2) a son, alive and well, aged 83. He is a musical conductor and composer by profession, and is described as of a quiet disposition, clever and highly strung. He is at present an organist and choirmaster, has published much sacred music, and even in his 83rd year has published several anthems. He married and had six children; his wife was the authoress of several books for children, and is described as being highly strung and very neurotic; she died aged 40 years. The first child, a son, was very clever, described as a genius in the obituary notices. He won scholarships and prizes, and had numerous degrees and honours conferred upon him by English and foreign universities. He died aged 34 from Bright's disease. He had two children, who are alive and well. Of the other members of this family, the three daughters and their offspring are alive and well. The remaining two sons were both musical conductors. Each had one healthy child; one of the former died aged 27 after operation for cerebral tumour, and the other died aged 35 from pneumonia. Throughout, this family shows a high degree of intelligence and talent in their respective professions.

(3), the daughter of (1), is described as nervous, highly strung and always eccentric, but she was a musical genius and the composer of some of the best known songs of the present day; she died aged 72 from dropsy. She married (4) an artistic designer who was highly religious, and who died aged 28 from tuberculosis. (The sister of this man also died from tuberculosis.) They had two children.

The eldest (6), a daughter, died aged 47 from diabetes; she was a confirmed alcoholic, very excitable, impulsive and passionate. She married and had three children, the eldest daughter and her three children are alive, normal and healthy; the second, a daughter (single), aged 39, is described as sulky and melancholic in temperament, and the son (not married) is a music-hall artist and is alcoholic.

The youngest (5), a son, and the father of our patient, at the age of five had a tubercular knee. He was a chronic alcoholic, and died at the age of 53 from cirrhosis of the liver. He was affectionate and highly religious, but very passionate; he was a musical genius, the author of numerous sacred and secular compositions, many of them being the most popular of the day; he was also a professor in one of the chief London academies. He married a gifted soprano and teacher of voice production. She is alive, aged 55, markedly

intelligent, highly strung and excitable. She came of a very good stock as is shown by the pedigree ; her parents are alive and well, both over 80 years of age, and all her ancestors were long lived and healthy. One of her nephews is one of the best known authors in America at the present time.

There were three children by this marriage, the eldest (7), a son aged 25, now in Cane Hill Asylum. He is congenitally deficient, mischievous, emotional, impulsive, spiteful, and passionately fond of music. The next child (8), a daughter, aged 22, is a gifted soprano. She has a daughter, who, although young, is described as being "exactly similar to (7)." The youngest (9) is a son (single), aged 21, who has always given trouble ; he is extravagant, passionate, and violent, alcoholic and a moral degenerate. He has also marked musical ability.

PEDIGREE II.

The following pedigree shows the apparent elimination of a marked insane taint by marriage into healthy stocks.

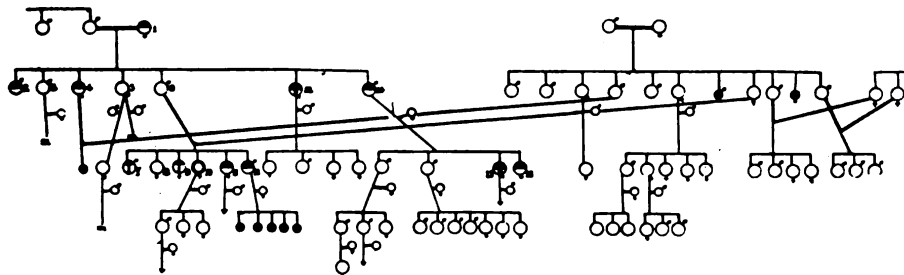


FIG. 2.—Half-black circles—*insanity*. Circle with deep rim—*nervous disease*. Small shaded circle—*died young*. T.—*tuberculosis*. S.—*suicide*.

In this pedigree the insanity commences as far as can be ascertained with (1) a woman whose first attack occurred during her fifth pregnancy, about the age of 44 ; nothing is known of her previous family history. She had several relapses subsequently, eventually dying at the age of 65. She was married into a family in which there is no history of alcohol, tubercle or insanity, her husband living to the advanced age of 92. There were seven children of the marriage ; (2) a son, who never married, was insane at intervals, the first attack occurring at the age of 25, and he eventually died at the age of 50 after several relapses in Bodmin Asylum, Cornwall ; (3) a son, married at the age of 50, died without offspring aged 80 ; (4) a daughter, who became insane after childbirth was in Bethnal House Asylum, aged about 40, and had several subsequent relapses. The child died aged one month. (It will be seen from the pedigree that she married into a family without taint and that her husband's

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sister married her brother.) (5) a daughter, who married twice and died of old age ; there was no issue of the first marriage, and the only daughter of the second in turn married but had no issue, and is now alive and well aged 50 ; (6) a son, died of old age at 79, married (4's) husband's sister ; there were six children, a son (7), unmarried, died aged 24 of consumption ; a daughter (8) single, alive and well, aged 63 ; a daughter (9) single, died aged 18 of consumption ; a daughter (10) who died, aged 50, of internal tumour ; she always suffered from neurasthenia, was married, and had three children all alive and well, one of whom married but has no children ; a daughter (11) who had an attack, stated to be hysteria, at the age of 20, and subsequently had several attacks of insanity, being under certificate for many years in Camberwell House and elsewhere, she married but had no children ; (12) a son, who is stated to have always been excitable, after years of business worry took to drink, and at the age of 54 was sent to Cane Hill Asylum, where he now is. He married and states that his wife had two premature children, both of which died, aged a few weeks ; she subsequently had numerous miscarriages. (The question of syphilis naturally arises. The patient denies infection. There were no external signs, and his blood gives a negative Wassermann re-action, but he admits the frequent risk of infection before marriage.)

(13) a daughter, who at the age of 45 became insane and within a few months committed suicide by throwing herself from the window. She was married and had four children, a son who went abroad and has been lost sight of, two daughters who died respectively aged 16 and 35 of typhoid and phlebitis ; a daughter who at the age of 45 is alive and well, but unmarried. (14) a son, insane at the age of 40 years, who on being released from Bethnal Asylum disappeared leaving no traces, he was married, his wife being now alive and well aged 80 ; there were four children, the first two have married and had children, several of these in turn married, one of them also having issue. The third child (15), a daughter, who married but had no issue, became insane at the age of 45, and after being in several asylums was discharged and committed suicide, aged 54, by hanging. The fourth child (16), a daughter, became insane at the age of 16 and has been under asylum care ever since.

It will be seen that the tainted members of this family had but scanty progeny, and the stock in the present generation is now apparently free from taint, the ages of these members varying from 18 to 35. I have carefully gone into their respective histories and occupations and find that without exception they are of a high degree of intelligence, and occupy responsible positions in their professions.

PEDIGREE III.

The following pedigree is of interest as three members of the present generation are now inmates of Cane Hill Asylum, and throughout the maternal stock there is admittedly a marked history of prolonged alcoholic abuse in nearly all the members. Tuberculosis figures in both maternal and paternal stocks, but, so far as can be ascertained, none of the present generation are affected :—

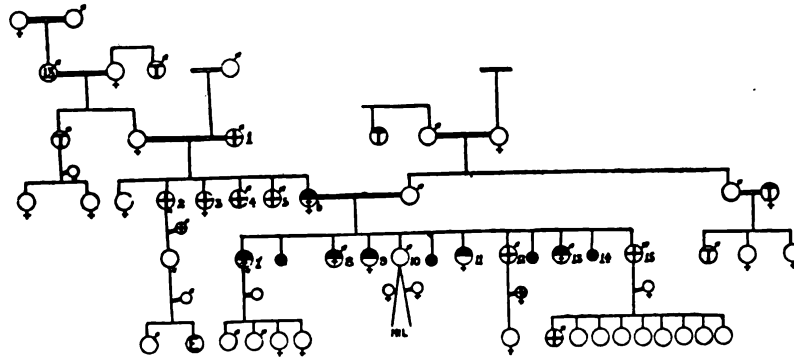


FIG. 3.—Half-black circles—*insanity*. Half-black circles with cross—*insane and alcoholic*. Circles in quadrants—*alcoholic*. T.—*tuberculosis*. E.—*epileptic*. Number in circle—number in family. Numbers outside circles—reference numbers.

The taint apparently first appears in (1) an only child whose father died young. The former was most excitable and of a passionate disposition and was a chronic alcoholic. At the age of 60 he was found dead in a chair (inquest heart failure). His wife lived to the age of 75, dying from cancer of the uterus. She had one brother who died from tuberculosis. Their mother also died from cancer of the uterus, and she had a brother who died, unmarried, from tuberculosis. The mother was the wife of the youngest of 13 brothers who were of Dutch origin, having been brought over from Holland by their father who was a man of wealth and standing, there was no history of taint of any kind in that family ; the children of (1) are as follows :—A daughter who was single, was normal and died of bronchitis, aged 70 ; (2) a daughter, always alcoholic, who married a man also addicted to alcohol. There was one daughter who in turn married and had two children, one now alive and well, the other (E) dying at the age of two years from fits ; (3) a daughter (alcoholic), always most eccentric and quite irrational, though never certified, single ; (4) a son (alcoholic), who was found dead, the cause of death being unknown ; (5) a son, alcoholic ; (6) a daughter (alcoholic), married, aged 25, was in Three Counties Asylum at the age of 28, suffering from puerperal mania ; 12 months after her discharge thence, she gave birth to what they described as the “bright
(16147)

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spot of the family " (10), she married into a healthy family, free from insanity and alcoholism, her husband being killed in a train accident aged 60 (he, however, had a brother who married, his wife dying from tuberculosis at the age of 60, after having given birth to three children, all of whom are unmarried). The son died of tuberculosis, but the two daughters are alive and well.

There were nine children and several miscarriages, the order of the latter being unknown. The children in order of seniority are as follows: (7) a daughter, who was in Wallingford Asylum at the age of 45 suffering from religious mania, afterwards becoming a melancholic, she is now alive and well aged 67; she was alcoholic, and also married a man who was addicted to alcohol; there are two sons and two daughters of the marriage, their ages varying from 25 to 15; they are all unmarried and all of a very hasty temper.

(8) a son, who at the age of 17 was in Three Counties Asylum for seven months, suffering from acute mania; he was bad tempered, restless and of poor intellect; he was addicted to alcohol and was found dead in bed, aged 35, the cause of death being stated to be bronchitis and heart trouble; he was unmarried. (9) a daughter, single, sent to Cane Hill Asylum 12 months ago, aged 44, suffering from acute melancholia, with strong suicidal tendencies; she admits that she had always been fond of drink; she has improved since admission but is still under continuous observation.

(10) a son, who is sound mentally and physically, but is and always has been a fair drinker; he has been twice married, but there are no children of either marriage; he was born 12 months after his mother's discharge from Three Counties Asylum.

(11) a daughter, single, aged 40, admitted to Cane Hill Asylum 12 months ago suffering from acute melancholia; she has made little improvement since admission. (12) a son, a confirmed alcoholic, who married a woman also addicted to alcohol; there is one daughter, aged 19 (unmarried), who is described as of a very quiet disposition. (13) a son, admitted to Cane Hill Asylum nine months ago, aged 32, suffering from acute melancholia with acute suicidal tendencies, he is of very poor physique, his appearance suggesting mental deficiency, he has for years been much addicted to alcohol; since admission he has greatly improved, but is quite unfit to face the world. (14) a son, who died aged two of measles. (15) a son, a confirmed alcoholic, who married and had nine children, the eldest of whom is in the army and has just recovered from a mental breakdown at the age of 24, the remaining eight are teetotalers, unmarried and well.

PEDIGREE IV.

The following pedigree is of interest in showing the transmission of an epileptic taint, with its reappearance in the present generation, probably owing to marriage into a stock affected by alcoholism and tuberculosis:—

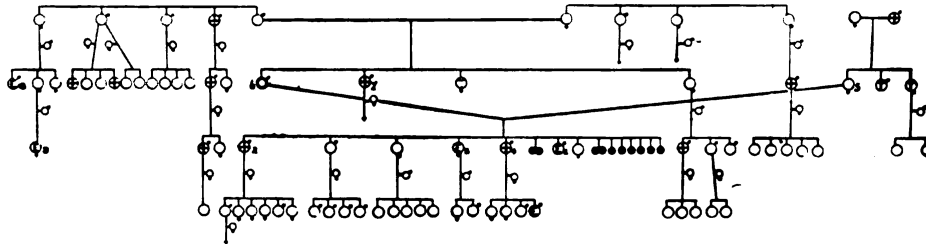


FIG. 4.—Circles in quadrants—*alcoholism*. Circle with deep rim—*nervous disease*. E.—*epilepsy*. T.—*tuberculosis*. Small shaded circles—*miscarriages or died in infancy*.

The patient (1) is one of seven children living, in addition to numerous children who died in infancy, mainly from convulsions. The latter are not in exact order of birth. He is an epileptic imbecile now aged 31 years, having been in Cane Hill Asylum since he was 29. His fits commenced when he was aged 10. He is unmarried. His eldest brother (2) is described as alcoholic, very violent and bad tempered; he is the father of six children, ages varying from 21 to $2\frac{1}{2}$ years, who are healthy and free from fits. The next brother is an abstainer; he has four children, ages varying from 17 to 8, and all the family are described as normal. The next is a sister who has five children from 15 to $2\frac{1}{2}$ years of age, all well and healthy. The next sister (3) has been subject to fits since she was 30; she is married and has two children aged 10 and 4 respectively, but these have had no fits and are described as being healthy and sharp. The following brother (4) is described as alcoholic, violent and bad tempered; he has four children of ages from 13 to 3; the youngest, a boy, is reported to have fits.

Maternal ancestry.—The mother (5) is described as nervous and melancholic. She had a brother and a sister who died from tuberculosis in adolescence; the sister was married and had two children. The maternal grandmother was healthy and lived to the age of 70 years, but the maternal grandfather was tubercular and a chronic alcoholic, eventually dying from delirium tremens at the age of 56.

Paternal ancestry.—The father (6) of the patient was a life abstainer, who is alive aged 73 years. He is described as being a somnambulist and of very nervous temperament. His brother (7) died at the age of 50 from delirium tremens, after prolonged alcoholic abuse; he was married but had no family.

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The next child, a sister, died aged 20 years from tuberculosis. The youngest of the family, a sister, married and had three children; nothing calls for comment regarding her children and grandchildren, except that her eldest son was alcoholic.

With regard to the paternal grandmother and her brothers and sisters, there is no history of insanity or epilepsy, and nothing calls for comment except that the only son of her youngest sister was a marked alcoholic. The other brother and sister were also married and had healthy families. The paternal grandfather was a steady, abstemious man, who died at the age of 67 from cerebral hæmorrhage. His brothers and sisters lived to good old ages; alcoholism figures in the families of two of them. His sister, however, by her marriage with a healthy man, who died at the age of 80, had three children. The eldest, a son (8), had fits from birth and died in a fit at the age of 40. The other two daughters had no fits, but one married, and her only child had fits from birth and is now in Exeter Asylum.

PEDIGREE V.

The following pedigree is of peculiar interest owing to the fact that the affected member of each family was an imbecile. The surviving members are apparently normal and healthy, and it would appear that there has been a segregation in a few members of all the unsound elements of the neuropathic inheritance:—

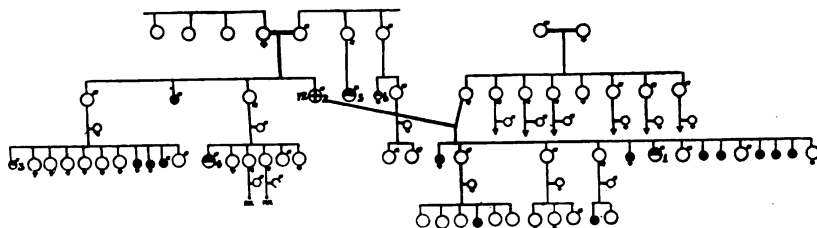


FIG. 5.—Half-black circles—*imbecility*. Circle in quadrants—*alcoholism*. Small shaded circles—*died in infancy*. E.—*epilepsy*. Small black circle—*miscarriage or still-born*.

The patient (1) is an imbecile aged 20 years, resident in Cane Hill Asylum. His serum is negative to the Wassermann test. He is one of seven surviving children; there were at least seven other pregnancies resulting in children dying in infancy mainly from convulsions or still-births. The surviving brothers and sisters and their children are healthy and apparently free from taint. One brother has five children living of ages varying from 13 to 1 year; another, three children of ages from 4 years to 3 months.

Maternal ancestry.—The mother of the patient is bright and intelligent,

and undoubtedly sound physically and mentally. She has four brothers and three sisters ; six of these are married and have large families, and there is no history of insanity, epilepsy, &c., tuberculosis or alcoholism concerning any member of this stock.

Paternal ancestry.—The father (2) of the patient was an habitual alcoholic, who died at the age of 52 from apoplexy. He is reported to have had fits as a child, but not in adult life. His eldest brother had 11 children, three of whom died in infancy from convulsions ; the first born was an imbecile (3) and died at the age of three years, and the surviving seven children are apparently physically and mentally sound ; they are all unmarried.

Concerning the remaining brother and sister of the father, the brother died from "convulsions" at the age of four years ; the sister married and had six children, the first born (4) is an imbecile from birth but has never been certified. He is now aged 40, and is quite helpless, being looked after at home ; the remainder of the children are apparently free from taint.

Regarding the paternal grandfather there is little known, as he deserted his wife after the four children were born and has not been heard of since. He, however, had a sister and brother who were both married ; the sister had an imbecile son (5), and the brother was father of a hydrocephalic idiot (6), his other child, however, was healthy and also his children. I was able to obtain no history of insanity, &c., concerning the paternal grandmother and her cofraternity.

PEDIGREE VI.

This pedigree shows the elimination of the neuropathic inheritance by anticipation and marriage into a sound stock, the surviving generations being sound physically and mentally.

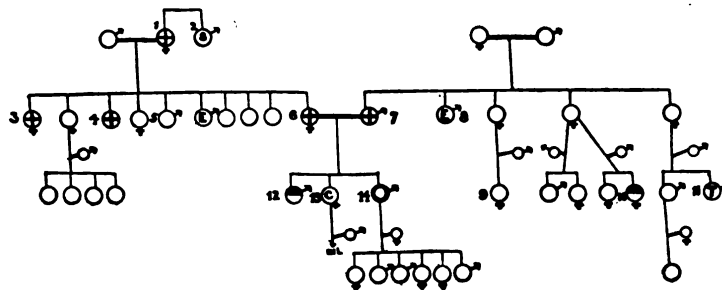


FIG. 6.—Half-black circles—insanity. Circles in quadrants—alcoholism. Circle with deep rim—nervous disease. E.—epilepsy. S.—suicide. T.—tuberculosis. Numbers for reference purposes.

The pedigree commences with (1) an alcoholic, who had a brother (2) who committed suicide by drowning. The former married a man described as eccentric, but of whom nothing else is known. There were 10 children of the

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marriage, a daughter (3), single, always alcoholic; a daughter who married and had four healthy children; (4) a son, alcoholic, unmarried; a daughter and a son healthy; then (5) a son, an epileptic, a patient in Darent Asylum; then three children of whom nothing is known, and the youngest (6), a daughter, a confirmed alcoholic; she married into a family with an insane taint. Her husband (7) is described as a moderate alcoholic, who died aged 65 of *complications*. He had a brother (8) single, an epileptic who died in Caterham Asylum; a sister who married and had one child (9) who died, single, aged 40, of diabetes. Another sister married twice; there were two children from the first marriage and two from the second, one of the latter (10) dying in Cane Hill Asylum aged 38. She was engaged to a man who committed suicide by shooting himself, and to this was attributed the patient's mental breakdown. The last daughter married and had a son, who died of consumption aged 28.

There were three children of the marriage of (6) and (7); a son (12) now a patient in Cane Hill Asylum (acute mania), first attack, admitted at the age of 23 years; (13) a congenital deficient, described as of low type and poor intelligence, who married but has no children; a son (14) who is said to have been treated for years for neurasthenia. He married; his wife came of a good stock and is of exceptionally good physique both mental and physical, and there have been six children of the marriage, all sound mentally, their ages varying from 26 to 10 years.

PEDIGREE VII.

The following pedigree shows the association of alcoholism and insanity in a stock; anticipation has occurred with the insane members with the result that the stock has practically come to an end:—

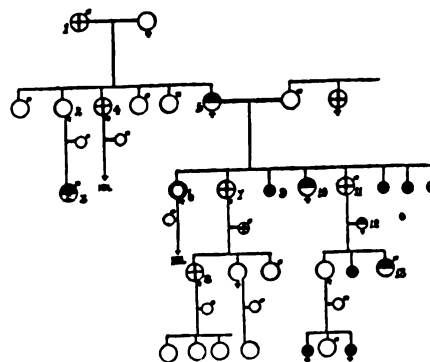


FIG. 7.—Half-black circles—insanity. Circles in quadrants—alcoholism. Small shaded circles—died young.

The pedigree commences with (1) a man much addicted to alcohol all his life, who married; his wife died aged 86, about whom no information can be obtained. They had six children; a son, about whom there was nothing of interest; a daughter (2) who married and had (3) an idiot child; a daughter (4) a confirmed alcoholic who married but had no children; then two children about whom nothing is known; and a daughter (5) married, who at the age of 20 was in St. Luke's Hospital suffering from milk fever; she had married a man who was a teetotaler and about whom there is nothing known except that he had a sister who was alcoholic. There were eight children of the marriage; a daughter (6), very excitable and eccentric, who died aged 68, was married but had no children; a daughter (7) always alcoholic, who married and had three children including (8) a daughter, who married and had three children all now alive and well; another daughter who married and has one child and a son unmarried, the latter all well; (9) a child which died in infancy; a daughter (10) who was taken to Cane Hill Asylum at the age of 21, a case of adolescent insanity dying at the age of 30, her first attack occurring at the age of 18 years, and she was previously in Peckham House and Bethlem Asylum; a son (11), very alcoholic, always of a very excitable temperament, and now decidedly mentally enfeebled. He married (12), who was a patient in Banstead Asylum at the age of 34 and died there aged 38, she is stated to have suffered from a very severe skin disease which she inherited from her father; she was informed that it was "English leprosy," but from the account given it might well be syphilis, as eventually her face was entirely eaten away; there were three children of the marriage, a daughter described as excitable and passionate, who married and had three children, a child born dead at full term but with a skin disease, and a son (13), now a patient at Cane Hill Asylum aged 31; he was aged 19 years at the time of first attack; he has always been excitable and passionate, and is now acutely maniacal; the cause of his mental breakdown is stated to be the breaking-off of his engagement, and, strangely enough, his fiancée herself comes of a very insane stock.

Summary.

The above pedigrees have been described as being of interest in themselves, but I feel that they are too few in number to justify any definite conclusions regarding the vast subject of insanity and heredity. These and other family histories I have obtained, however, have suggested that :—

1. When an insane taint manifests itself in a family, it appears to be confined to one or more members, leaving the remainder and their progeny (should they make a normal healthy marriage) free from taint.

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2. The affected members have but scanty progeny, owing to their being affected by insanity early in life and thereby prevented from propagating, or should they be able to marry their fertility appears to be limited to a great extent.

3. A latent tendency in a member of a tainted stock apparently can be revived by the marriage of that member into a stock devitalised by marked alcoholism, tuberculosis, syphilis or other racial poisons.

4. Epilepsy does not appear to conform so well with the foregoing remarks regarding insanity, for an epileptic taint may become manifest in any member of a stock, even of unaffected lines, and may proceed for many more generations than is the case with insanity.

Hereditary Resemblance in the Fissures of the Cerebral Hemispheres.

By EDGAR SCHUSTER, M.A., D.Sc., Fellow of New College, Oxford.

(From the Pathological Laboratory, Claybury Asylum.)

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I.—INTRODUCTION.

The knowledge, developed in recent years, that the fissures in the surface of the cerebral hemispheres indicate in some cases, at any rate, the boundaries of regions differing from one another in structure and function, renders the study of their hereditary resemblances one of particular interest. The extreme difficulty of obtaining the brains of persons related to one another has prevented much attention from being given to the subject hitherto, and in all probability the time is still far distant in which it will be possible to examine the hemispheres of all members of a family consisting of three or more generations. Meanwhile, the most complete and satisfactory material hitherto available is being collected from the London County Asylums by Dr. Mott, and I should like here to express my warm gratitude to him for affording me the opportunity of studying it. Dr. Mott's enquiries have enabled him to ascertain that more than 15 per cent. of the inmates of the London County Asylums, who together equal in numbers the population of a fair sized town, are connected to some other inmate, past or present, by ties of relationship. The cards on which the "related" cases are recorded number now more than 3,000. The brains of these persons, when they die, are whenever possible preserved, so that gradually a magnificent collection is accumulating. It will, however, be many

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years before sufficient are available for statistical study, and appears to me doubtful whether Mendelian analysis will ever be practicable, as the families dealt with must necessarily be incomplete. Therefore, at present, one must be contented with individual comparisons, which may have a certain value as indicating whether hereditary resemblance exists or not, even whether it is strongly or faintly marked, although they cannot form a basis for measuring the amount of correlation between relatives of different degrees with regard to the cerebral characters, nor indicate whether the hereditary transmission is Mendelian or otherwise.

The present paper is a first instalment of a work which may take some years to complete. It contains comparisons between the fissures in the hemispheres of two pairs of relatives; (1) a pair of brothers; (2) a mother and daughter. The comparisons are made in detail in the text, and a table is appended in which the relations of some of the more important fissures to one another are analysed. The headings and arrangement of the table are taken for the most part from similar comparative tables contained in the great work of Gustav Retzius, "*Das Menschenhirn*."

It has been thought advisable before proceeding to the descriptions to include a review of the most important work of a similar nature that has been published, and also to give in detail the nomenclature which has been employed in this paper, or will be employed in future instalments; for the sake of indicating as clearly as possible what fissures and gyri are denoted by the various names, a list of synonyms has been added, which, however, makes no pretence to completeness.

The descriptions are illustrated by tracings from photographs, modified so as to accentuate the more important and deeper fissures. In the best of original photographs of a brain shallow grooves often appear as conspicuous as the deepest fissures, while the arrangement of the lights and shades in some parts is such that important sulci are rendered practically invisible. Hence tracings such as here included, being fairly diagrammatic, give in many ways a truer representation of the essential features.

The photographs themselves were prepared in the Pathological Laboratory of the London County Asylums, Claybury.

II.—PREVIOUS WORK.

The most thorough and important work on the inheritance of the surface configuration of the cerebral hemispheres is that of Karplus.*† His material

* Karplus, J. P. "*Über Familienähnlichkeiten an des Grosshirn furchen des Menschen. Arbeiten aus dem Neurologischen Institute an der Wiener Universität*," Bd. XII, p. 1, 1905.

† Karplus, J. P. "*Zur Kenntniss der Variabilität und Vererbung am Zentralnervensystem des Menschen und einiger Säugethiere*." Leipzig und Wien, 1907.

was derived from 26 families, from each of which two or more members were available for examination, having died within a day or two of one another. In the majority of the cases in which it was possible to examine the brain both of parent and child the parent was the mother and the child either new born or not yet born. Many of the sets of twins or triplets were also new born or foetal, and in some cases the foetal brains were not sufficiently developed to be comparable with those of adults. Crime, accident and infectious disease were the causes of death which rendered other of the brains available for study.

The author's method of presenting the material thus collected is clear and sufficient, though, considering how much detail has to be dealt with, it is brief and free from verbosity. It consists essentially of a tabular comparison of the conditions of the more important fissures in each member of the family, to which are appended notes pointing out the more striking points of similarity.

The following among others are conclusions drawn :—

“Inheritance of the fissures of the brain does take place. The members of a family may be, as everybody knows, extraordinary alike in general appearance and in their psychical characters, so much so that they may be confused one with another. In other cases the fact that they belong to the same family betrays itself in a number of small traits and features without there being any marked general resemblance. Thus it is also with the brains. The general configuration is in some cases similar, while in others agreement of countless smaller variations in several members of the same family bears witness to the hereditary transmission of the fissural arrangement.

“A second not unimportant fact appears to me to arise from my observations. It concerns the relations of the two hemispheres to one another. The two halves of a brain are in general like one another. The brain is either large or small, long or short, it has broad or narrow gyri, and fissures more or less numerous, and it shows all these characters both in the right side and in the left. But with regard to particular points, every brain shows differences between the two hemispheres, especially in the characters here studied, namely, the length, depth, interruption and anastomoses of the several fissures. Now it appears from our researches that the two halves show an independence in respect to their hereditary transmission. Peculiarities of the right hemisphere in one member of a family are found also on the right hemisphere in others, those on the left side in one member are reproduced on the left side in others.”

In connection with the conclusion reached by Karplus that there is inheritance of the fissures of the brain, he makes the following remarks :—If

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one considers single varieties, it is at once clear, that a variety will be the more convincing evidence of inheritance, the more often it is present in one family and the less frequently it occurs in general. . . . But a numerical statement concerning the degree of resemblance would be too unreliable, because our knowledge of the variations of fissures in general is still much too incomplete, and the statements made by various authors on this point differ very much from one another.

Certain numerical summaries may be made from the author's own tables, which, although they are not based on a sufficient number of observations to make them a satisfactory statistical measure of inheritance, appear to me to form a useful supplement to the test of his own conclusions. Below are given one or two examples.

(1) The special point dealt with is whether the sulcus centralis does or does not form an anastomosis with the sulcus precentralis superior. Seventeen hemispheres of children are available for comparison with the corresponding hemispheres of one of their parents. In 13 cases the anastomosis mentioned was absent, while in four it was present. In only one of the 13 cases in which it was absent in the children was it present in the parents; while three times out of four its presence in the children was associated with presence in the parents.

In studying the resemblance between the offspring of a single pair of parents, for which it will be convenient to use the word "siblings" (a translation of the German "geschwister"), introduced by Prof. Karl Pearson, it is necessary to take each sibling in turn and compare him or her with the other siblings of the same family. There are 50 hemispheres available for tabulation in this way, in 26 of them the sulcus precentralis superior was connected with the sulcus centralis, and in 24 it was not; in 18 cases out of the 26, presence of this anastomosis in the one sibling was associated with its presence in the other, and in 16 cases out of 24 it was absent in both members of pair, while only in 8 cases was it absent in the one and present in the other, or present in the one and absent in the other.

TABLE 1.

	Parents—		Total.
	Anastomosis present.	Anastomosis absent.	
Children—			
Anastomosis present	3	1	4
Anastomosis absent	1	12	13
Total	4	13	17

TABLE 2.

	First sibling—		Total.
	Anastomosis present.	Anastomosis absent.	
Second sibling—			
Anastomosis present	18	8	26
Anastomosis absent	8	16	24
Total	26	24	50

The members may be seen more clearly in the tables given above, of which the verbal statement made above is intended as an explanation. A corresponding statement will not be made with reference to the other examples chosen.

After giving the necessary caution that the numbers are very small for statistical purposes, it is permissible to remark that in so far as they go they demonstrate a resemblance between parents and children, and between siblings with regard to the character dealt with.

(2) The character here dealt with is the extent the upper or inner end of the sulcus centralis. It may cut the superomesial border, it may just reach it, or it may fall short of it. In making the tables the cases in which the border is just reached are classed with those in which the fissure does not extend so far and are contrasted with the cases in which angle of the hemisphere is cut and the mesial surface reached. Two tables have been drawn up corresponding to those given in the preceding section.

TABLE 3.

Showing resemblance between parents and children with regard to the upper extent of the sulcus centralis.

	Parents—		Total.
	Sulcus centralis cuts the superomesial border.	Sulcus centralis reaches or falls short of the border.	
Children—			
Sulcus centralis cuts the superomesial border	6	6
Sulcus centralis reaches or falls short of the superomesial border	3	8	11
Total	9	8	17

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TABLE 4.

Showing resemblance between siblings with regard to the upper extent of the sulcus centralis.

	First sibling—		Total.
	Sulcus centralis cuts the superomesial border.	Sulcus centralis reaches or falls short of the border.	
Second sibling—			
Sulcus centralis cuts the superomesial border	26	8	34
Sulcus centralis reaches or falls short of the border	8	8	16
Total	34	16	50

It will be seen by inspecting Tables 3 and 4 that a particular condition of the sulcus centralis in the parent is many times more often associated with the like condition in the child than with the contrasted condition, and that the same statement holds true, *mutatis mutandis*, with regard to siblings.

(3) The sulcus precentralis may appear as a continuous fissure as it may be divided into two portions—S. precentralis superior and inferior, the most usual arrangement, or it may fall into more than two segments.

(Karplus does not always state expressly whether the sulcus precentralis forms a continuous fissure or not. Where it is not stated I have taken it to mean that the fissure is not continuous but falls into two or more segments. Where, however, a sulcus precentralis is referred to it is assumed that the continuity of the fissure is implied.)

TABLE 5.

Showing resemblance between parents and children with regard to the continuity or discontinuity of the sulcus precentralis.

	Parents—		Total.
	Sulcus precentralis continuous.	Sulcus precentralis discontinuous.	
Children—			
Sulcus precentralis continuous	3	3
Sulcus precentralis discontinuous	4	11	15
Total	7	11	18

TABLE 6.

Showing resemblance between siblings with regard to the continuity and discontinuity of the sulcus precentralis.

—	First sibling—		Total.
	Sulcus precentralis continuous.	Sulcus precentralis discontinuous.	
Second sibling—			
Sulcus precentralis continuous	4	7	11
Sulcus precentralis discontinuous....	7	34	41
Total	11	41	52

The same remarks which are made with regard to Tables 1 to 4 are equally applicable here.

(4) The sulcus postcentralis, like the sulcus precentralis, may be in the form of a continuous fissure, or may fall into two separate pieces, S. postcentralis, superior and inferior. Sometimes the two portions are divided by an almost superficial gyrus ; in this case I have counted them as separate.

TABLE 7.

Showing resemblance between parents and children with regard to continuity and discontinuity of the sulcus postcentralis.

—	Parents—		Total.
	Sulcus postcentralis continuous.	Sulcus postcentralis not continuous.	
Children—			
Sulcus postcentralis continuous	9	4	13
Sulcus postcentralis not continuous	1	3	4
Total	10	7	17

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TABLE 8.

Showing resemblance between siblings with regard to the continuity or discontinuity of the sulcus postcentralis.

	First sibling—		Total.
	Sulcus postcentralis continuous.	Sulcus postcentralis not continuous.	
Second sibling—			
Sulcus postcentralis continuous	28	11	39
Sulcus postcentralis not continuous	11	11
Total....	39	11	50

Table 7 shows considerable resemblance between parents and children with regard to this character. Continuity of the fissure in the parent is associated with a like condition in the child in 9 hemispheres out of 17, discontinuity in 3, while in only 5 cases are unlike conditions met with.

It cannot be said that Table 8 shows any resemblance between siblings.

If the results from all the four characters are considered together it will be seen that a considerable degree of resemblance is shown throughout between parents and children, and in three cases out of the four between siblings. The fourth case is probably a chance result due to the smallness of the numbers of observations. Thus, in so far as my tabulations of Karplus' data go they certainly confirm his conclusion that there is inheritance of the fissures of the brain.

Other work on the subject has been published by Spitzka,* but as Karplus includes summaries of this, I have not thought it necessary to give an account of it.

A paper by Waldeyer entitled "Gehirne Von Zwillingsfruchten Verschiedenen Geschlechte,"† does not deal with hereditary resemblances but with sexual differences.

* *E.g.* Spitzka. Hereditary Resemblance in the Brains of three Brothers, "American Anthropologist," Vol. VI, 1904.

† "Zeitschrift f. Ethnologie," Bd. XL, 1908.

III.—NOMENCLATURE* OF FISSURES AND GYRI, WITH NOTES AS TO THEIR SYNONYMS.

(The abbreviations used in the figures are also given.)

A. <i>Fissures separating Lobes of the Hemisphere:</i>		Synonyms.
Fissura Sylvii	<i>Fsy</i>	
Ramus posterior ascendens ..	<i>rpa</i>	Episylvian. Wilder. §
Ramus posterior descendens ..	<i>rpd</i>	Hyposylvian. Wilder.
Ramus anterior ascendens ..	<i>ra</i>	Presylvian. Wilder.
Ramus anterior horizontalis ..	<i>rh</i>	Subsylvian. Wilder.
Sulcus centralis	<i>c</i>	Fissure of Rolando.
Fossa parieto occipitalis ..	<i>fpo</i>	
Connected with this are—		
Sulcus limitans praecunei ..	<i>lpr</i>	Adoccipital. Wilder.
Sulcus paracalcarinus ..	<i>pro</i>	
(These form respectively the anterior and posterior boundaries of the arcus intercuneatus.)		
Arcus intercuneatus ..	<i>arc int</i>	
Incisura parieto occipitalis ..	<i>ipo</i>	
Sulcus calcarinus	<i>cal</i>	
B. <i>Lobus Frontalis:</i>		
(1) Sulci—		
Sulcus precentralis superior ..	<i>prs</i>	Supercentral. Wilder.
Sulcus precentralis inferior ..	<i>pri</i>	Precentral. Wilder.
‡ Ramus horizontalis	<i>h</i>	

* The nomenclature used by Gustav Retzius ("Das Menschenhirn," Stockholm, 1896) has been followed except when dealing with the occipital lobe, where that adopted by Elliott Smith has been substituted. (Elliott Smith, "Journal of Anatomy and Physiology," Vol. XLI, page 198, 1907; also "Records of the Egyptian Government School of Medicine," Vol. II, page 125, 1904.)

§ Wilder, "Reference Handbook of Medical Sciences," Vol. VIII, page 107, 1889, and Supplement, page 99, 1895; used also by Spitzka, "Transactions of the American Philosophical Society," Vol. XXI, page 175, 1908.

‡ Cunningham, "Royal Irish Academy, Cunningham Memoirs," Vol. VII. (16147)

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		Synonyms.	
Sulcus precentralis intermedius	<i>prm</i>	Sulcus precentralis medius.	Cunningham.
Sulcus precentralis marginalis (Cunningham).	<i>marg</i>	(When this fissure is present Retzius describes the condition as a division into two portions of the sulcus precentralis superior.)	
Sulcus precentralis medialis (Eberstaller).	<i>pr med</i>	Sulcus paracentralis.	Schwalbe.*
Sulcus frontalis superior ..	<i>fs</i>	Inflected sulcus.	Wilder.
		Superfrontal.	Wilder.
		Sulcus frontalis primus.	Cunningham.
Sulcus frontalis medius ..	<i>fm</i>	Medifrontal.	Wilder.
Sulcus frontalis mesialis ..	<i>fms</i>		
Sulcus frontalis inferior ..	<i>fi</i>	Sulcus frontalis secundus.	Cunningham.
		Sub frontal.	Wilder.
Sulcus fronto-marginalis ..	<i>fma</i>	Orbito frontal.	Wilder.
		(The fronto-marginal mentioned by Spitzka is a very variable fissure lying in the mesial surface of the hemisphere in the superior frontal gyrus.)	
Sulcus radiatus	<i>r</i>		
Sulcus diagonalis	<i>d</i>		
Sulcus subcentralis anterior ..	<i>sca</i>	Sulcus inferior transversus.	Eberstaller.
		Transprecentral.	Wilder.
Sulcus cinguli	<i>sc</i>	Sulcus calloso marginalis.	
		(The posterior portion of this sulcus is called by Wilder "paracentral," the anterior portion "supercallosal.")	
Sulcus rostralis superior ..	<i>rts</i>		
Sulcus rostralis inferior ..	<i>rti</i>		
Sulcus rostralis transversus ..	<i>rtt</i>		
Sulcus olfactorius	<i>olf</i>		
Sulcus orbitalis.. ..	<i>orb</i>		
(2) <i>Gyri</i> —			
Gyrus centralis anterior		Ascending frontal gyrus.	
Gyrus frontalis superior.			
Gyrus rectus.		(The orbital surface of the gyrus frontalis superior.)	
Gyrus frontalis medius.			

* Quoted from Retzius.

Gyrus frontalis inferior—

Divided into three portions,
where it lies superficially—

- (1) Pars superior (opercularis).
- (2) Pars intermedia (triangularis).
- (3) Pars anterior (orbitalis).

Synonyms.

(Retzius notes that it has an under surface opposed to the temporal lobe and an inner surface opposed to the insula, on both of which he distinguishes various gyri.)

C. *Lobus Insularis* (Reilii) :

(1) Sulci—

Sulcus circularis insulæ
(Schwalbe*).

Sulcus centralis insulæ (Guldberg*)

Sulcus longitudinalis. Marchand.*

Sulcus præcentralis insulæ.

Sulcus brevis (anterior and posterior).

(2) Gyri—

Lobus posterior insulæ

Postinsula. Wilder.

Divided into—

Gyrus centralis posterior
primus.

Gyrus centralis posterior
secundus.

Lobus anterior insulæ.. .. .

Preinsula. Wilder.

Divided into—

Gyrus centralis anterior in-
sulæ.

Gyrus brevis primus.

Gyrus brevis intermedius.

Gyrus brevis secundus.

Gyrus accessorius

Gyrus transversus insulæ. Eberstaller.*

D. *Lobus Parietalis* :

(1) Sulci—

Sulcus postcentralis superior ..

pos Postcentral. Wilder.

Sulcus postcentralis inferior ..

poi Subcentral. Wilder.

Sulcus subcentralis posterior..

scp Transpostcentral. Spitzka.

Retrocentralis transversus. Eberstaller.*

* Quoted from Retzius.

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Sulcus interparietalis proprius	<i>ip</i>	Synonyma.
Sulcus occipitalis transversus	<i>tr</i>	(Wilder calls the anterior portion of the sulcus interparietalis proprius the parietal fissure and its posterior portion together with the sulcus occipitalis transversus the paroccipital fissure. Cunningham describes as the interparietal sulcus both postcentral fissures together with the sulcus interparietalis proprius. He distinguishes four elements: Sulcus postcentralis superior and inferior, a ramus horizontalis = Wilder's parietal fissure, a ramus occipitalis = Wilder's paroccipital fissure without the sulcus occipitalis transversus.)
Sulcus parietalis superior ..	<i>ps</i>	Transparietal. Wilder.
Sulcus intermedius primus (Jensen* and Eberstaller*).	<i>ima</i>	
Sulcus intermedius secundus ..	<i>imp</i>	
Sulcus subparietalis	<i>sp</i>	Precuneal. Wilder. = Sulcus
Sulcus precunei	<i>pc</i>	subparietalis and sulcus precunei.
(2) Gyri—		
Gyrus centralis posterior		Ascending parietal gyrus.
Lobulus parietalis superior—		
Consisting of—		
(a) On the mesial surface—		
Praecuneus, which may be divided into—		
Gyrus praecunei anterior.		
Gyrus praecunei posterior.		
(b) On the lateral surface—		
Gyrus arcuatus anterior.		
Gyrus arcuatus medius.		
Gyrus arcuatus posterior.		
Lobulus parietalis inferior—		
Consisting of—		
Gyrus supramarginalis.		
Gyrus angularis.		
Gyrus parietalis inferior posterior.		
Operculum parietale.		

* Quoted from Retzius.

E. Lobus Temporalis :-

Synonyms.

(1) Sulci—

Sulcus temporalis superior ..	<i>Ts.</i>	Parallel Fissure. Supertemporal. Wilder. (The ramus ascendens is sometimes called sulcus angularis.)
Sulcus temporalis transversus superior.		
Sulcus temporalis medius ..	<i>Tm</i>	Meditemporal. Wilder.
Sulcus temporalis inferior ..	<i>Ti</i>	Subtemporal. Wilder.
Fissura collateralis	<i>col</i>	
Fissura rhinica	<i>rh</i>	Postrhinal or amygdaline. Wilder.
Sulcus rhinencephali inferior ..	<i>sri</i>	
Sulcus sagittalis gyri fusiformis.		
Sulcus lingualis	<i>lsi</i>	Sulcus limitans areæ striatæ inferior. Elliott Smith.
Sulcus paracollateralis.. ..	<i>p. col</i>	Sulcus limitans areæ parastriatæ inferior. Elliott Smith. (Retzius only distinguishes one fissure in the gyrus lingualis, which he calls Sulcus sagittalis gyri lingualis.)
Sulci temporales transversi		Transtemporals. Wilder.

(2) Gyri—

Gyrus temporalis superior.
Gyrus temporalis medius.
Gyrus temporalis inferior.
Gyrus temporalis polaris.
Gyrus lingualis.
Gyrus fusiformis.

F. Lobus Occipitalis :-

Sulci—

Sulcus calcarinus proprius ..	<i>cal</i>	Stem or anterior calcarine fissure. Cunningham.
Sulcus retrocalcarinus.. ..	<i>im</i>	Sulcus intrastriatus mesialis. Elliott Smith.
Ramus verticalis	<i>imv</i>	
Sulcus calcarinus externus (of Cunningham).	<i>iml</i>	Sulcus intrastriatus lateralis. Elliott Smith.
Sulcus cunei	<i>lss</i>	Sulcus limitans areæ striatæ superior. Elliott Smith. Sulcus sagittalis inferior cunei. Retzius. Intracuneal. Wilder.

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Synonyms.

Sulci polares, superior et inferior.	<i>pol s</i>	Polarsulci. Bolton.
	<i>pol i</i>	
Sulcus lunatus	<i>lun</i>	"Affenspalte."
Sulcus occipitalis lateralis (of Eberstaller).	<i>ol</i>	Sulcus praelunatus. Elliott Smith.
Sulcus occipitalis paramesialis	<i>o. prm</i>	

IV.—POINTS OF SIMILARITY IN THE BRAINS OF TWO BROTHERS, G. D. AND H. D.

Summary of Clinical Notes.

G. D. Aged 56. Was admitted to Hanwell, November 16, 1896. A jobmaster by occupation, and apparently up to the time of his attack had been fairly successful in his business. He was married and had a daughter. The attack of insanity followed a serious illness, apparently pneumonia and drinking. There was loss of memory of recent events and various delusions. Thus the certificate states: "Says he is at the present time in his brother's house, imagines he went to Paris yesterday and after leaving France he drove a horse and also rode horseback to Hornsey and back." He did not improve mentally; in fact the notes indicate a progressive dementia, and he died November 7, 1910, of chronic Bright's disease and pneumonia.

H. D.—Became insane at the age of 22. He was first an inmate of Bethlem, then of Haywards Heath Asylum, and in June, 1875, he was admitted to Hanwell. Up to the time of his first attack, September, 1874, he was a potman, steady, quiet and temperate in his habits, fond of reading and intelligent. There is a history of having had fits in infancy, but there is no family history of insanity.

When admitted he had numerous delusions of a non-systematised nature, sometimes of exaltation, at other times of persecution. He appears from the notes also to have had hallucinations of hearing, and after some years he passed into a state of chronic dementia. He was in Hanwell until his death at the age of 59 in 1910, having been an inmate 35 years. The cause of death as ascertained at the post-mortem was bronchitis. Probably the case would now be called dementia præcox.

COMPARISON OF HEMISPHERES.

Left hemispheres.—The *sylvian fissure (Fsy)* has in both cases two anterior and two posterior rami. In G. the two anterior rami (*ra* and *rh*) are fairly well developed and join the sylvian fissure by a common stem; in H. they are barely visible from the lateral surface and open into a fairly conspicuous gap in the operculum, through which a portion of the insula may be seen.

The *sulcus centralis (c)* in both cases cuts the superomesial border and joins the sylvian fissure by means of the *s. subcentralis anterior (sca)*.

Frontal lobe.—The *sulcus praecentralis inferior* (*pri*) in both cases at its lower end falls short of the sylvian fissure; it has a well developed vertical stem, the top of which joins a *ramus horizontalis* (*h*) which is turned backwards so as to lie in an almost vertical direction.

The *sulcus praecentralis superior* (*prs*) is a moderately developed curved fissure, with its convexity directed forwards.

The *sulcus frontalis superior* (*fs*), well developed in both cases, is divided into two segments in G., but continuous in H., it joins S. praecentralis superior at its posterior end.

The *sulcus frontalis medius* (*fm*) is also well developed in both cases; it is a continuous fissure in G., terminating anteriorly in the middle segment of the sulcus frontomarginalis (*fma*); in H. it is broken up into at least three pieces, the posterior of which lies transversely, joining S. praecentralis inferior at its outer end.

The *sulcus frontalis inferior* (*fi*) in both cases forms an incomplete union with S. praecentralis inferior at its posterior end; it is partially separated from it by a gyrus, which is completely submerged in G., but almost on the surface in H. In G. it runs forwards in superficial continuity to join the *sulcus radiatus* (*r*) in front, but two elements separated by a deep annectant gyrus are in reality present. In H. it consists of a simple segment ending in front in a shallow transverse groove which bears some resemblance to a *sulcus radiatus*. The latter is, however, present as an independent fissure, and is indeed particularly well developed, thus compensating for the small extent of the anterior branches of the sylvian fissure.

There is a strongly marked *sulcus diagonalis* (*d*) present in both cases, which joins the sylvian fissure below, ending freely above.

The *sulcus frontomarginalis* (*fma*) is present in both cases divided into three segments.

Parietal lobe.—The *sulcus postcentralis inferior* (*poi*) is separate from S. postcentralis superior in both cases, but forms a direct connection with the ramus posterior ascendens (*rpa*) of the sylvian fissure, a connection which is fairly deep in G. but shallow in H.

The arrangement of the sulcus postcentralis superior (*pos*) is somewhat different in the two brains correlated with a difference in the anterior portion of the *sulcus interparietalis* (*ip*). In G. the latter extends backwards between the two postcentralis sulci, thus reducing the downward extent of S. postcentralis superior, from which it is entirely separate. An annectant gyrus rising almost to the surface divides it from the upper end of S. postcentralis inferior. In H. the lower end of the sulcus interparietalis is bent downwards in front of the upper end of S. postcentralis inferior (*poi*); it is entirely separate

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from the latter but is connected by means of a shallow groove running at right angles to it about 2 cm. from its lower end with the superior post-central fissure.

The *sulcus parietalis superior* (*ps*) falls into two portions, of which one lying behind the upper extremity of the *S. postcentralis superior* (*pos*) is connected over a deep annectant gyrus with the *Sulcus praecuneus* (*pc*). The position of the other piece differs; in G. it lies behind the *S. postcentralis superior* (*pos*) with which it is superficially connected above, while below it establishes a somewhat deeper communication with the *Sulcus interparietalis* (*ip*); in H. it lies in front of the *sulcus postcentralis superior*.

The arrangement of the *sulcus interparietalis* (*ip*) shows a considerable similarity in the two brains. The differences in the position of the anterior end have already been dealt with. In both cases the fissure is divided in the middle by a gyrus which rises almost to the surface, the posterior segment being prolonged forward on the mesial side of the anterior portion. The posterior segment in both cases ends in the *S. transversus occipitalis* (*tr*) in the usual manner. The *sulcus intermedius primus* (*ima*) in both cases joins the anterior portion. The *S. intermedius secundus* (*imp*) joins the anterior segment in G. and the posterior segment in H.

In the *Praecuneus* the *sulcus praecuneus* (*pc*) is represented by three fairly well developed fissures in G., of which the anterior and also the posterior join the *S. subparietalis* (*sp*) below, while the middle one is connected with the *S. parietalis superior* (*ps*). In H. there are two well-developed fissures, of which the posterior joins the *sulcus subparietalis* (*sp*), and the anterior the *sulcus parietalis superior* (*ps*), while two shallow grooves lying in front of the latter correspond with the most anterior of the three present in G. The *sulcus subparietalis* in both cases forms a superficial connection with the *sulcus cinguli* (*sc*).

The *arcus intercuneatus* (*arc. int.*) and its limiting sulci is well developed in both cases and lies near the surface, in G. its anterior limb is actually exposed.

Temporal lobe.—The *sulcus temporalis superior* (*Ts*) shows some curious points of similarity and some curious differences in the two hemispheres. In G. it falls completely into three segments; of these the anterior joins a deep sulcus which lies behind the first transverse gyrus of Heschl, and thus appears to make a connection with the sylvian fissure. In H. an anterior segment is also present, and is separated from the posterior portion of the fissure by an annectant gyrus lying not very far from the surface. The sulcus which lies behind the first transverse gyrus of Heschl is deep in this case also, and the first segment of *S. Temporalis superior* sends out a branch towards it, which, however, fails to join it.

A *sulcus Temporalis transversus superior* is present in both cases.

Occipital lobe.—It is in the occipital lobe in which perhaps the most marked agreement can be observed. In both cases there is a well-marked *sulcus lunatus* (*lun*) 2 to 3 cm. from the occipital pole, but the striate area does not quite reach its lip, stopping some 7 mm. behind it. In both a straight *S. occipitalis lateralis* (*ol*) stretches forwards and connects the sulcus lunatus with a segment of the sulcus Temporalis medius (*Tm*). On the mesial surface the *sulcus retrocalcarinus* (*im*) runs practically the same course in both cases and ends posteriorly without branching, but whereas in G. it stretches on to the lateral surface, in H. it is not prolonged over the occipital pole. The limiting sulci of the striate area, namely, the *sulcus cuneus* (*lss*) above and the sulcus lingualis (*lsi*) below, are well-marked and follow closely the course of the *S. retrocalcarinus* (*im*). This arrangement is practically identical in the two cases. The upper and lower limiting sulci of the parastriate area, namely, *S. occipitalis paramesialis* (*o. prm*) and *S. paracollateralis* (*p. col*) are both well marked, and a considerable similarity is shown in respect to the former. It lies almost entirely in the mesial surface, in practically the same position in the two brains, but is longer in G. than in H.

The *sulcus collateralis* (*col*) is an additional point of agreement; it is a continuous fissure which ends in front and behind in a bifurcation and is joined by the sulcus paracollateralis. In G. a connection is also established with the anterior end of the *S. calcarinus* (*cal*), but this connection is quite superficial, although a casual examination of a photograph of the hemisphere might lead one to suppose that it is deep.

The *sulcus polaris inferior* (*pol. i*) is well marked in both cases, and the *sulcus calcarinus externus* (*iml*) presents the same form in both subjects—a short straight fissure with its posterior extremity bifid and thus forming a compensating arc round the posterior end of *S. retrocalcarinus*.

Right hemispheres.—The sylvian fissure (*Fsy*) shows practically the same arrangement in both cases with regard to both its anterior and its posterior rami. The only difference shown is that in G. the two anterior rami (*ra* and *rh*) join it by means of a very short common stem, in H. they are independent. There are two large transverse gyri of Heschl present, and the fissure separating them (*fH*) is a deep one and thus conspicuous on the lateral surface of the hemispheres.

The *sulcus centralis* (*c*) in both cases just reaches the superomesial border. Near its upper extremity it enters into practically the same arrangement with the upper or mesial segment into which the *sulcus precentralis superior* is divided, *sulcus precentralis marginalis* (*marg*). The latter is in both cases a triradiate fissure, and its lower posterior limb is separated from the sulcus

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centralis by a narrow gyrus which is slightly below the surface in H., yet as it remains visible from the surface the fissures do not appear to anastomose; while in G. as it is not visible from the surface, the fissures are apparently in continuity.

Frontal lobe.—In the precentral fissures the same elements may be distinguished in both cases, but the connections which they make one with another differ. The *S. precentralis marginalis* (*marg*) has already been referred to. There are also present a short *S. precentralis superior* (*prs*), a *S. precentralis intermedius* (*prm*), and a *S. precentralis inferior* (*pri*) provided with a ramus horizontalis (*h*). The ramus horizontalis in both cases runs obliquely upwards and forwards; it is continuous with the *S. precentralis inferior* in G., but separated from it in H., and in both cases it is joined by the *S. frontalis inferior* (*fi*). The *sulcus precentralis inferior* (*pri*) in both cases joins the sylvian fissure without the intervention of the *S. subcentralis anterior*. The *sulcus precentralis intermedius* (*prm*) at its lower end joins *h* near the posterior extremity of the latter in G., but is separated from it in H.; at its upper end it joins the *S. precentralis superior* in H., but in G. is separated from it by a slightly submerged gyrus. This is a case in which a tabular record of the anastomoses would show considerable differences in the two brains, although the conditions present are practically the same.

The *sulcus frontalis inferior* (*fi*) is in both cases connected at its posterior end with *h* near to the point at which the latter joins or almost joins the *sulcus precentralis inferior*, but in G. complete continuity is prevented by an annectant gyrus lying not far from the surface. At its anterior end it joins the *sulcus radiatus* (*r*) in G., but falls short of it in H. The *sulcus radiatus* (*r*) is a well developed fissure over 4 cm. in length, arranged in a very typical way so as to bisect the angle formed by the two anterior rami of the sylvian fissure.

The *sulcus frontalis superior* (*fs*) falls into two pieces in G., into three pieces in H. The posterior piece in both cases is continuous with the *S. precentralis superior* at its posterior end; at its anterior end it is superficially continuous with the *S. frontalis medius* (*fm*) in G.

Parietal lobe.—The two *sulci postcentrales* form a continuous fissure in both cases, though their point of union is clearly shown by a deep annectant gyrus in G. The *S. interparietalis* (*ip*) joins the *S. postcentralis superior* (*pos*), but a secondary connection with the *S. postcentralis inferior* (*poi*) is also present in G.'s brain through the agency of another element which may be regarded as a part of the *sulcus intermedius primus* (*ima*). A similar element is present in H. but does not form the connection mentioned above.

The *sulcus interparietalis* (*ip*) is completely divided into two parts in H. The superficial gyrus which separates them having its counterpart in a deep

annectant present in the same position in G. The posterior segment of *ip* ends behind in both cases in the *sulcus occipitalis transversus* (*tr*), and in front it sends up a mesial branch ending in a bifurcation which forms the anterior boundary of the gyrus arcuatus posterior.

The *sulcus parietalis superior* (*ps*) is divided into an upper and a lower portion in both cases.

The *arcus intercuneatus* (*arc. int.*) presents the same peculiarity in both cases. It stands up from the bottom of the fossa parieto-occipitalis (*fpo*) as a solid wedge-shaped mass which can be seen end on from the lateral surface. When the hemisphere is viewed from above the arcus appears as a triangular area with its apex directed towards the mesial border, bounded in front and behind by fissures which look like two diverging branches of the fossa parieto-occipitalis, and continuous laterally with the surface of the gyrus arcuatus-posterior. The posterior of the two fissures is the *S. paracalcarinus* (*prc*), and the anterior the *incisura parieto-occipitalis* (*ipo*). The sulcus limitans praecunei is sunk in the fossa.

Temporal lobe.—The fissures of the temporal lobe show some points of similarity in the two brains, a *S. temporalis transversus superior* is present in both, and the *S. temporalis superior* (*Ts*) is a continuous fissure. Its anterior portion lies near the sylvian fissure and parallel to it in the middle temporal gyrus is an additional fissure (*Tx*) about 4 cm. in length. The ascending branches of the sulci temporales superior and medius (*Ts* and *Tm*) are connected near their lower ends by a transverse fissure, which is about 23 mm. long in G. but only 5 mm. long in H.

The two brains have some common features in the arrangement of the *S. collateralis* (*col*). In both cases there is an obliquely placed anterior portion which is joined to the main fissure in H. but in G. is separated off by a superficial gyrus rhinencephalo-fusiformis anterior. The *S. paracollateralis* is present and is united at its anterior end with the *S. collateralis*; posteriorly it ends in a transverse member in H., which is present in G. but as a separate element.

Occipital lobe.—The characters of the occipital lobe show more divergence than similarity, in H. the arrangement of the fissures is much the same as in the left hemisphere, and the stria of Gennari extends on to the lateral surface. In G. the arrangement is quite different, and therefore not worth describing in detail. The stria of Gennari extends only as far as the occipital pole.

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V.—POINTS OF SIMILARITY IN THE BRAINS OF A MOTHER AND DAUGHTER,
S. R. AND I. R.

Summary of Clinical Notes of the Mother and Daughter.

S. R.—Aged 65. Admitted to Hanwell 2.1.1907, under the following certificate :—“She is very talkative, restless and disturbing to patients; sleeps badly, wandering about collecting rubbish. She says she hears explosions in the ward and does not know when she will be blown up. She has been made ill since she has been here.” Her daughter says she has been strange for 20 years. She wanders out of doors and goes to house agents to buy large houses and shops whereas the family is practically penniless. She collects rubbish and hides it, and plays with lighted lamps.

She is the youngest of a family of three and was married at the age of 17. She has had nine children born alive, none born dead, two miscarriages. No history was obtainable concerning her family antecedents except that her mother lived to the age of 84 and was quite normal. The patient had a son who committed suicide at the age of 23 and a daughter who is now in the asylum. I. R. was born about the time S. R. was first noticed to be strange in her behaviour. Another married daughter who visited her was thought by the medical officer to be a neuropath.

Delusion of persecution persisted, and the notes frequently refer to her delusion that an attempt had been made in the infirmary to blow her up with dynamite. The notes indicate that she is subject to periods of maniacal excitement. She became gradually demented, developed tuberculosis and died of that disease April, 1910.

I. R.—Servant. Aged 16. Single. Admitted to Hanwell, October, 1901; died December 2, 1911. The medical certificate states that “She is unmanageable and requires supervision. Assaults patients in the ward. Swears at the nurses. Indecently exposes herself.” A sister has given the information that the patient was of an uncertain temperament. She had a blow on the head when nine years of age. “Patient was simple from a babe and though a lovable little thing, we soon found she could not learn, and though she was often quite docile and easy to manage she would have attacks of *stubbornness*, and to an outsider would appear to be a rude and insolent girl but *we* knew it was the mind.”

After admission it is stated that “she has occasional attacks of *petit mal*.” She was regarded as a weak-minded imbecile subject to frequent outbursts of excitement of a very violent character. 3.12.1906.—A note states that “she still has periods of excitement, when she is abusive to everyone. When she is quiet she is pleasant and converses.” The notes suggest to my mind that she

was a congenital high grade epileptic imbecile in whom the epilepsy was manifested by attacks of *petit mal* occasionally, but much more frequently by psychical equivalents of epileptic fits in the form of attacks of excitement and destructiveness.

On the evening of November 29, while dancing, she was seized with severe abdominal pains and "shrieked spasmodically." All the symptoms of acute intestinal obstruction are related in the notes, and on December 2 laparotomy was performed and 3 or 4 feet of strangulated small intestine was found ; there was a large quantity of blood-stained fluid in the abdomen ; but death occurred within 12 hours.

PORTRAITS OF I. R. AND S. R.



I. R.

S. R.

The photographs of the mother and daughter show, not only a likeness in physiognomy, but in posture of head. Whereas the daughter's expression does not indicate mental depression, the mother's face shows a marked overaction of the grief muscles ; there is evidence of depression of the angles of the mouth and of the corrugators supercillii frontalis and pyramidalis nevi, with this physiognomical manifestation of mental depression there is mingled excitement, especially the eyes show this. In fact the photograph of the patient gives one the idea that she is suffering with maniacal depressive insanity or agitative melancholia. The expression of the daughter shows none of the marked emotional characteristics of the mother's, although the features show a pronounced likeness. Her physiognomy may be well associated with the character given by her sister. A pleasant, good-looking girl, but the weak-mindedness and lack of highest control is not indicated. The history shows

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that her morbid mental state was periodic and of a psychical epileptic character.

COMPARISON OF HEMISPHERES.

Left hemisphere, frontal lobe.—The *sulcus precentralis inferior* (*pri*) shows in both the same characteristic T-shaped arrangement. In the daughter the *sulcus frontalis inferior* (*fi*) appears to join the anterior part of the horizontal limb (*h*) of *pri*, but is in reality separated from it by a deep annectant gyrus. A corresponding gyrus is present in the mother but lies on the surface.

The *sulcus precentralis superior* (*prs*) at its lower end joins the horizontal limb (*h*) of *S. præcentralis inferior*, and shortly above this gives off a backwardly directed branch which joins the *sulcus centralis* superficially in the daughter just above the inferior genu; it just falls short of that fissure in the mother. The upper part of the superior precentral fissure runs forwards in both cases, thus permitting the ascending frontal convolution to open out into a broad triangular area, in which is placed obliquely another short fissure which might be identified as the *sulcus precentralis marginalis* (*marg*). This fissure is connected posteriorly with the *sulcus centralis* (*c*) in the mother, but just falls short of it in the daughter. Its relation with the upper end of the superior precentral is not the same in both cases, being parallel to it in the mother, and forming in the daughter what Retzius describes as a transverse compensating sulcus.

The *sulcus frontalis superior* (*fs*) is in both cases a continuous fissure joining *prs* posteriorly; and there is also considerable resemblance with regard to the degree of development of the *sulcus frontalis mesialis* (*fms*).

Perhaps the most striking point of similarity in the frontal lobe is the development of the *sulcus frontomarginalis* (*fma*). It is in both cases divided into three portions, of which the lateral one (*fma 3*) extends far backwards, parallel to the orbital border. The *sulcus radiatus* (*r*) and the *sulcus diagonalis* (*d*) are in both cases poorly developed.

Parietal lobe.—The *sulcus postcentralis superior* (*pos*) is in both cases a long well-developed fissure which approaches the *sulcus centralis* at its upper end and then runs parallel with it for some distance, thus forming the posterior boundary of the somewhat narrow upper portion of the ascending parietal gyrus.

In the mother it cuts the superomesial border and ends in close relations with the *sulcus cinguli*. In the daughter it terminates in a bifurcation a little distance from the border, and a separate element appears in the place corresponding to that occupied by its mesial end in the mother, this element being in continuity with the *sulcus cinguli*.

Its lower end forms a very shallow connection with the *sulcus interparietalis* in the daughter and just fails to do so in the mother.

The *sulcus postcentralis inferior* (*poi*) is in both cases superficially continuous with the *sulcus centralis* at its upper end; its lower end joins the sylvian fissure through the agency of an intimate connection with the *sulcus subcentralis posterior* (*scp*) in the daughter; in the mother the latter sulcus is independent, terminating above just in front of the inferior postcentral. The *sulcus interparietalis* (*ip*) is in both cases a continuous fissure; its mesial branch which forms the anterior boundary of the gyrus arcuatus posterior appears to be continuous with the incisura parieto-occipitalis, though in reality separated from it by a submerged gyrus. In the mother the relation between the incisura and the main parieto-occipital fissure is peculiar, since the arcus intercuneatus in which it lies is superficial, thus the incisura appears as a small fissure quite distinct from the mesial fossa parieto-occipitalis, instead of being apparently its lateral continuation, as is the usual arrangement. In the daughter, although the elements present are essentially the same and bear similar relations to one another, they present a very different appearance in that the arcus intercuneatus is sunk in the fossa parieto-occipitalis.

The arrangement of the fissures in the lobulus parietalis inferior presents a considerable degree of similarity. In both cases small sulci form an arch round the ramus posterior ascendens of the sylvian fissure (*rpa*); behind these may be found the *sulcus intermedius primus* (*ima*) of Eberstaller, which is continuous above with the *sulcus interparietalis*. Behind this again the ramus ascendens of the *sulcus temporalis superior* (*Ts*) extends so far upwards that it almost joins the interparietal fissure. A considerable degree of resemblance may be seen in the arrangement of the ascending branch of the *sulcus temporalis medius* (*Tm*), a fairly straight well developed fissure which runs upwards and backwards to end in the angle formed at the point of origin of the outer limit of the *sulcus occipitalis transversus* (*tr*). In the triangular area which bounded in front by ascending branch of the superior temporal, and behind by the corresponding branch of the middle temporal, lie a lateral branch of the interparietal representing the *sulcus intermedius secundus* (*imp*), and a small secondary sulcus.

The praecuneus is noticeably larger in the daughter than in the mother. The occipital lobes also do not bear any striking resemblance to one another, but agree in that the stria of Gennari does not extend on to the lateral surface.

In the temporal lobe the anterior portion of the *sulcus temporalis superior* (*Ts*) is separated off from the posterior portion, an arrangement which Retzius found in 29 per cent. of the hemispheres examined by him. In the daughter the two segments communicate with one another by means of the third segment of the *sulcus temporalis medius* (*Tm* 3). Considerable similarity is shown in the arrangements of the first three segments of the latter fissure.

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Right hemisphere.—In the right hemisphere fewer points of resemblance may be discovered than in the left.

In the *frontal lobe* the *sulcus precentralis inferior* (*pri*) in both cases is T-shaped, the upper portion of the vertical stem is bent backwards in such a way that the morphological ramus horizontalis (*h*) comes to lie in an almost vertical position. Its lower (posterior end) cuts obliquely across the ascending frontal convolution, and in the daughter almost reaches the sulcus centralis.

In both cases the pars triangularis of the inferior frontal convolution is large as the two anterior rami (*ra* and *rh*) of the sylvian fissure join it independently. The other parts of the gyrus are correspondingly reduced.

The gyrus frontalis superior on the lateral surface is broad and divided longitudinally by a very well developed *sulcus frontalis mesialis* (*fms*). The arrangement of the posterior end of this convolution in the daughter is somewhat peculiar and worthy of special mention, although it bears very little resemblance to that of the mother. The sulcus praecentralis superior (*prs*) is much reduced, and has the appearance of being merely a bifurcated end of the *sulcus frontalis superior* (*fs*). Its lower end is in continuity with the sulcus centralis (*c*). Above it lies a *sulcus precentralis marginalis* (*marg*) continuous with the posterior segment of the sulcus frontalis mesialis (*fms*), and the upper end of this too joins the sulcus centralis. The ascending frontal convolution is thus completely traversed by two separate fissures in its upper portion and indeed can hardly be distinguished as such in this region.

In the *parietal lobe* the *sulcus postcentralis superior* (*pos*) is in both cases continuous with the *sulcus postcentralis inferior* (*poi*), and the *sulcus interparietalis* (*ip*) joins them over a deep annectant gyrus. In the daughter the inferior postcentral communicates with the sylvian fissure through the agency of the *sulcus subcentralis posterior* (*scp*). The latter sulcus is well developed in the mother also.

The gyrus supramarginalis in the mother presents a curious appearance as the ramus posterior ascendens (*rpa*) of the sylvian fissure runs backwards and establishes a superficial connection with the corresponding portion of the sulcus temporalis superior (*Ts*). The daughter's brain in this region has been too much damaged to enable me to say with certainty whether this identical condition is present, but so far as one can see the arrangement is very similar. In any case the sulcus intermedius primus (*ima*) is represented by an insignificant lateral branch of the sulcus interparietalis, below which a couple of secondary fissures, bearing in both cases much the same appearance, are present.

The *sulcus parietalis superior* (*ps*) is in both cases a well developed H-shaped fissure.

LIST OF ILLUSTRATIONS.

1. Left hemisphere, lateral aspect. G. D.
2. " " " " H. D.
3. " " mesial " G. D.
4. " " " " H. D.
5. Right " lateral " G. D.
6. " " " " H. D.
7. Both h. mispheres, viewed from above. G. D.
8. " " " " H. D.
9. Left hemisphere, lateral aspect. S. R. (mother).
10. " " " " I. R. (daughter).
11. Right " " " S. R. (mother).
12. " " " " I. R. (daughter).
13. Both hemispheres, viewed from above. S. R. (mother).
14. " " " " I. R. (daughter).

LIST OF ABBREVIATIONS USED IN FIGURES.

Arranged in Alphabetical Order.

(Not all the abbreviations given below are used in this portion of the paper now appearing.)

arc int	= Arcus intercuneatus.	prm	= S. precentralis intermedius.
c	= S. centralis.	pr med	= S. precentralis medialis.
cal	= S. calcarinus.	prs	= S. precentralis superior.
col	= S. collateralis.	ps	= S. parietalis superior.
fpo	= fossa parieto-occipitalis.	ol	= S. occipitalis lateralis.
Fay	= Fissura Sylvii.	olf	= S. olfactorius.
fi	= S. frontalis inferior.	o prm	= S. occipitalis paramesialis.
fm	= S. frontalis medius.	orb	= S. orbitalis.
fma	= S. fronto-marginalis.	r	= S. radiatus.
fms	= S. frontalis mesialis.	ra	= R. anterior ascendens of Sylvian Fissure.
h	= R. horizontalis of S. frontalis inferior.	*rh	= R. anterior horizontalis of Sylvian Fissure.
im	= S. retrocalcarinus.	rpa *	= R. posterior ascendens of Sylvian Fissure.
ima	= S. intermedius primus.	rpd	= R. posterior descendens of Sylvian Fissure.
iml	= S. calcarinus externus.	*rh	= fissura rhinica.
imp	= S. intermedius secundus.	rti	= S. rostralis inferior.
imv	= R. verticalis of S. retrocalcarinus.	rts	= S. rostralis superior.
ip	= S. interparietalis proprius.	rtt	= S. rostralis transversus.
ipo	= incisura parieto-occipitalis.	sc	= S. cinguli.
lpr	= S. limitans praecunei.	sea	= S. subcentralis anterior.
lsi	= S. lingualis.	sep	= S. subcentralis posterior.
las	= S. cunei.	sp	= S. subparietalis.
lun	= S. lunatus.	sri	= S. rhinencephali inferior.
marg	= S. precentralis marginalis.	Ti	= S. temporalis inferior.
pc	= S. praecunei.	Tm	= S. temporalis medius.
p col	= S. paracollateralis.	tr	= S. occipitalis transversus.
poi	= S. postcentralis inferior.	Ts	= S. temporalis superior.
pos	= S. postcentralis superior.		
pol i	= S. polaris inferior.		
pol s	= S. polaris superior.		
pri	= S. precentralis inferior.		

* This abbreviation is used for two fissures, but no confusion can arise as they are seen only in different views of the hemisphere.

166 *Hereditary Resemblance in the Fissures of the Cerebral Hemispheres.*

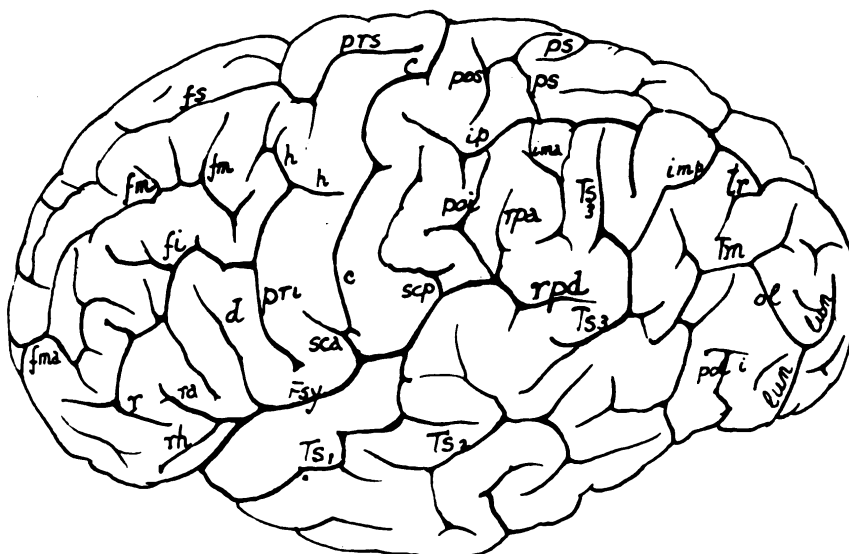


FIG. 1.—Left Hemisphere, G. D.

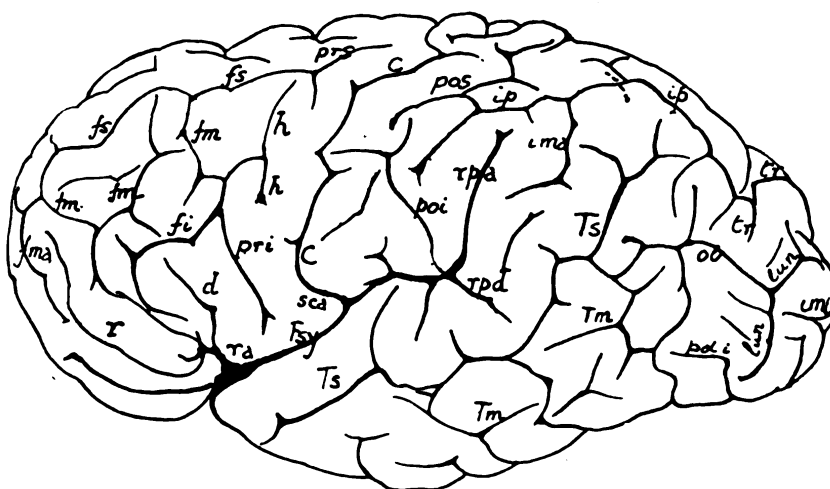


FIG. 2.—Left Hemisphere, H. D.

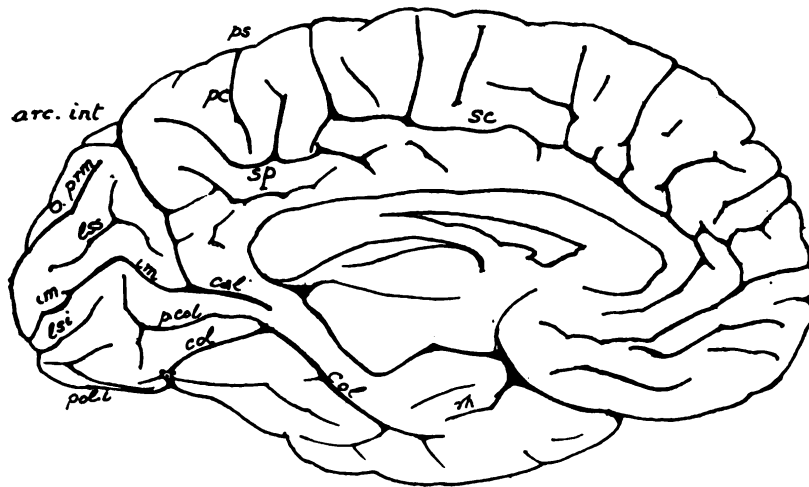


FIG. 3.—Left Hemisphere, G. D.

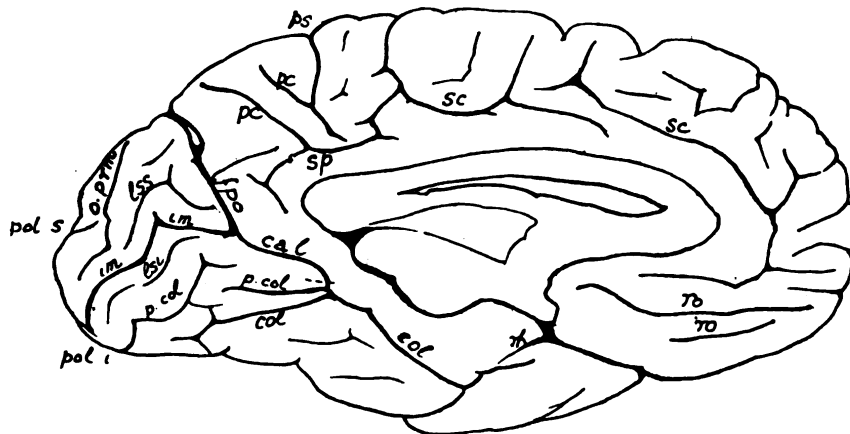


FIG. 4.—Left Hemisphere, H. D.

168 *Hereditary Resemblance in the Fissures of the Cerebral Hemispheres.*

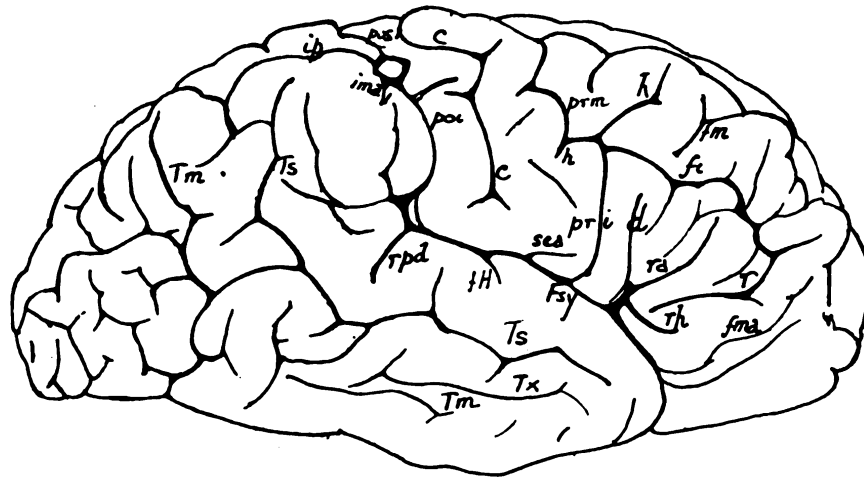


FIG. 5.—Right Hemisphere, G. D.

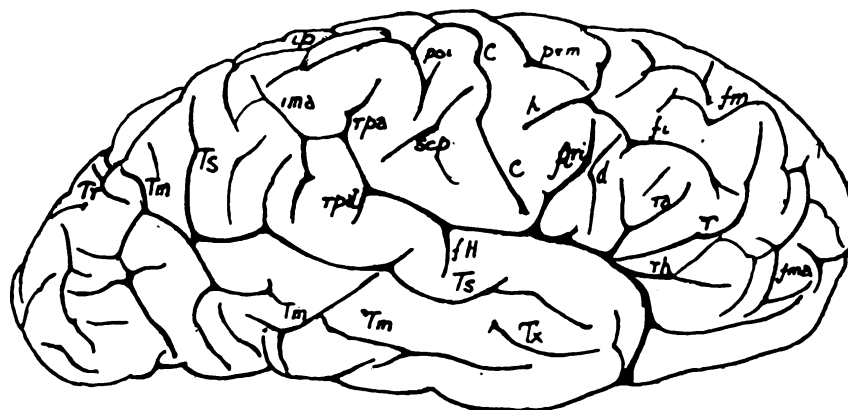


FIG. 6.—Right Hemisphere, H. D.

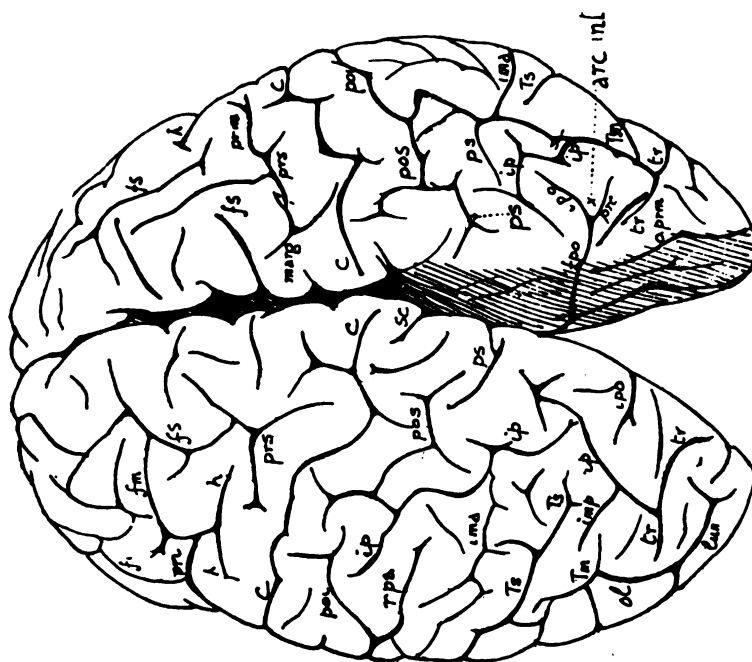


FIG. 8.—Cerebral Hemispheres from above, H. D.

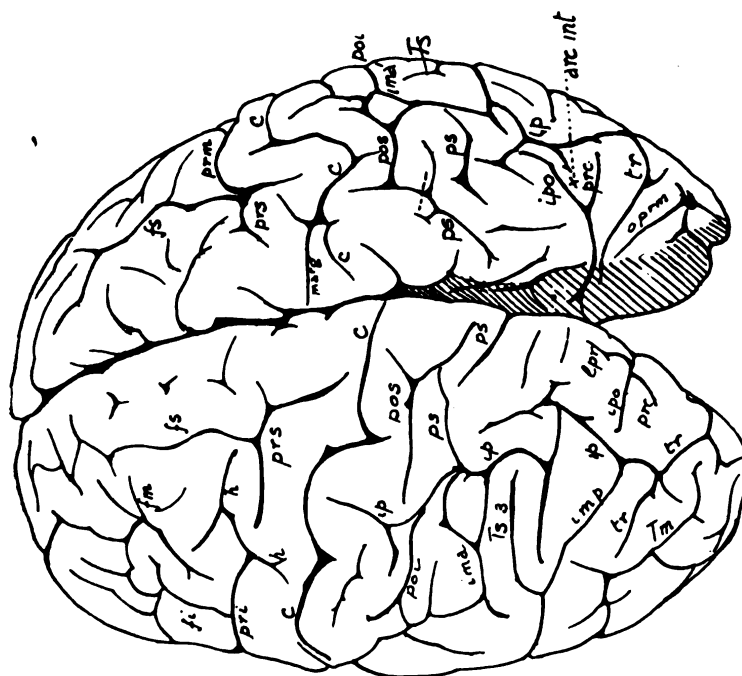


FIG. 7.—Cerebral Hemispheres from above, G. D.

170 *Hereditary Resemblance in the Fissures of the Cerebral Hemispheres.*

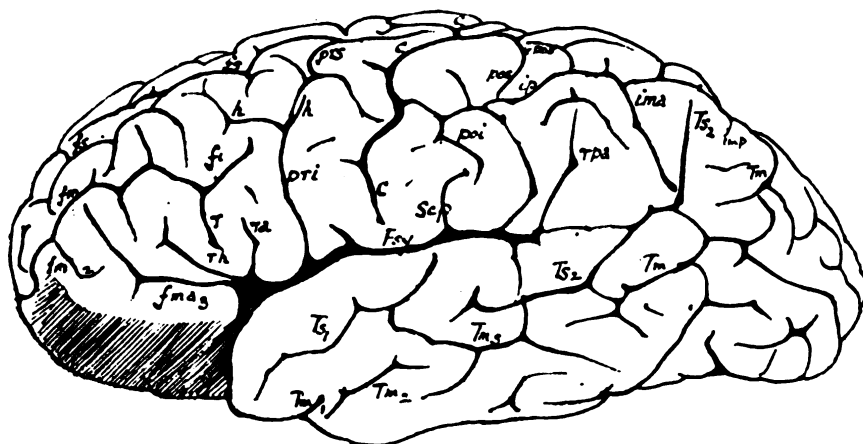


FIG. 9.—Left Hemisphere, S. R. (mother).

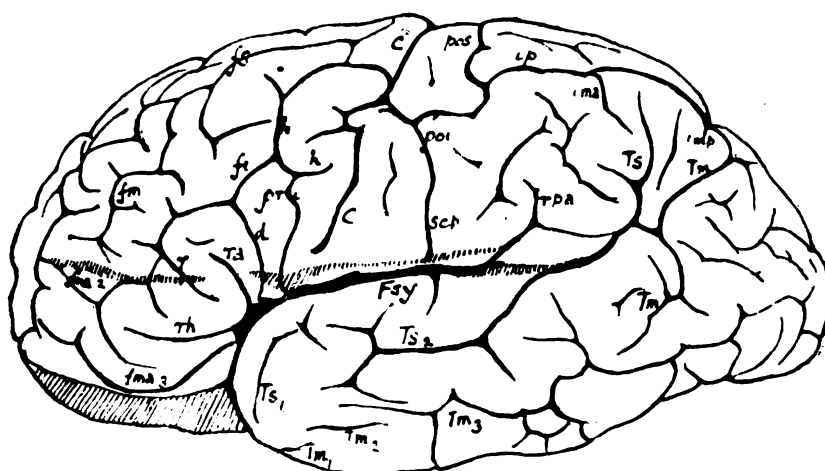


FIG. 10.—Left Hemisphere, I. R. (daughter).

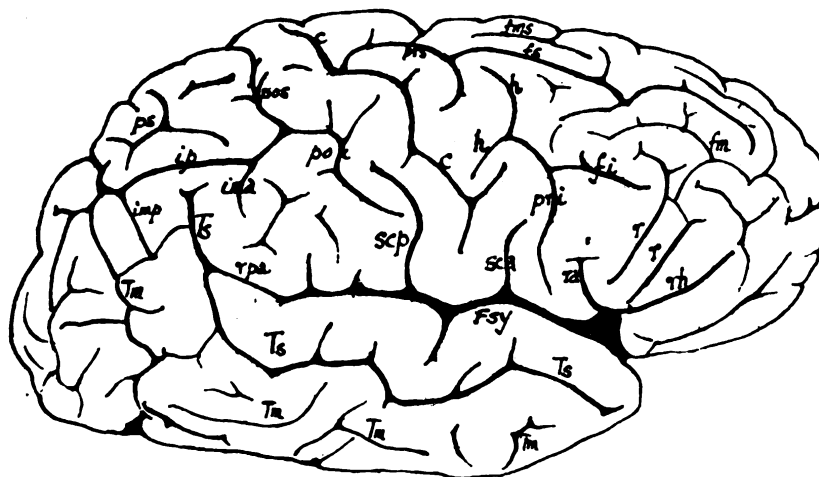


FIG. 11.—Right Hemisphere, S. R. (mother).

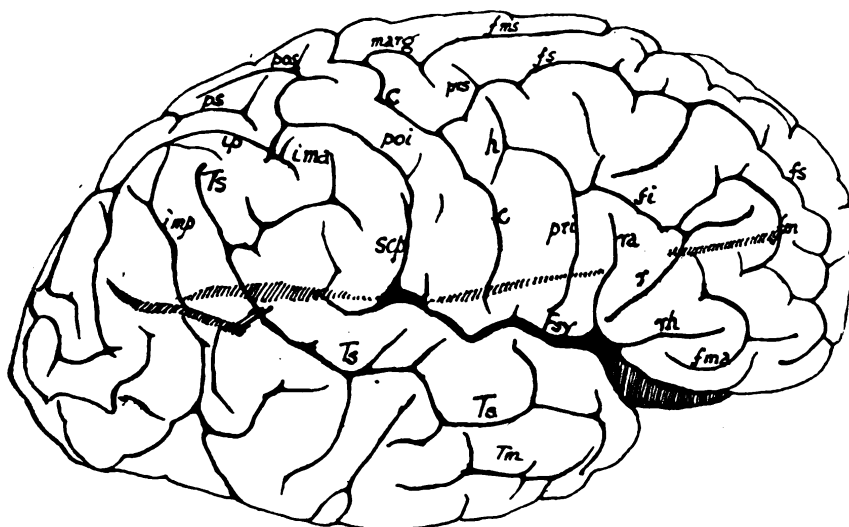


FIG. 12.—Right Hemisphere, I. R. (daughter).



-Arcus Intercuneatus

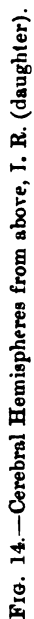


FIG. 14.—Cerebral Hemispheres from above, J. R. (daughter).

Description of the Brain of a Malay.

By EDGAR SCHUSTER, M.A., D.Sc., Fellow of New College, Oxford.

Clinical Notes.

B. A. I. (a Malay), admitted to Claybury Asylum February 23, 1912. Aged 35 years. First attack of insanity. Occupation, seaman-cook.

He is a native of Kmala Lampor, and has been in England about one year, mainly in hospitals, the Dreadnought Seaman's Hospital and others.

He was admitted suffering from melancholia with homicidal tendencies.

While in the asylum he became more quiet and his mental condition greatly improved, but he was suffering from phthisis and he gradually became weaker and died June 4, 1912.

Post mortem notes and measurements :—Height, 5 feet 6 inches. Chest, 29 inches.

Skull from occiput to root of nose, 17 inches. Calvaria, $20\frac{1}{2}$ inches. Root of ear to root of ear over parietal eminence, 12 inches.

Calvaria, inside greatest width, $5\frac{1}{2}$ inches ; length inside, 6 inches ; outside greatest width, $5\frac{3}{4}$ inches ; longitudinal, $6\frac{1}{2}$ inches. Shape, asymmetrical. Right half of calvaria larger than left.

The *affenspalte* appears to be well marked. Cerebellum is exposed owing to insufficient parietal development.

Laryngeal and pulmonary tuberculosis.

LEFT HEMISPHERE.

FISSURES SEPARATING LOBES OF THE HEMISPHERE.

Sylvian fissure (Fsy).—The *ramus anterior ascendens (ra)* and the *ramus anterior horizontalis (rh)* join the fissure by a common stem. Posteriorly the fissure ends in a sharply up-curved *ramus posterior ascendens (rpa)*, 23 mm. in length, and a short downwardly directed *ramus posterior descendens (rpd)*. Along its upper border the following connections are made : the sulcus diagonalis (*d*) runs into it a short distance behind the point at which the two anterior branches are given off, and through the sulcus centralis posterior (*scp*)

a communication is effected with the sulcus postcentralis inferior (*poi*). Along its lower border two short downward branches (*Ttr*) are given off, which mark the forward and hindward boundaries of the anterior transverse gyrus of Heschl.

The *sulcus centralis* (*c*) above just reaches the supermesial border, below it falls short of the sylvian fissure by about 5 mm. Its anterior wall is raised into two well marked gyri which interlock with corresponding gyri on the posterior wall. The position of these is indicated superficially by well marked bends in the course of the fissure and by two short backwardly directed, to one short forwardly directed, branch.

An apparent anastomosis with the posterior limb of the lower bifurcation of the sulcus precentralis superior (*prs*) is in reality quite superficial.

The *fossa parieto-occipitalis* (*fpo*) extends for about 20 mm. on to the lateral surface, below it is continuous with the sulcus calcarinus (*cal*). The gyrus cuneus is very poorly developed and hardly seems to cross the floor of the fissure.

The *sulcus calcarinus* (*cal*) and the *sulcus retrocalcarinus* (*im*) form a continuous fissure joined by the fossa parieto-occipitalis. Posteriorly it bends round on to the lateral surface and there ends in a well marked *ramus verticalis*. The two gyri cuneolinguales do not interfere with the continuity of the fissure; their positions are indicated by swellings on its walls, which do not cross its floor.

The *fissura collateralis* (*col*) is a deep fissure running continuously from its anterior extremity near the temporal pole to the point at which posteriorly it joins the sulcus lingualis (*lsi*). About 18 mm. in front of this it gives off a branch (*col a*) which runs outwards over the temporal surface; 12 mm. in front of this again another branch (*col b*) is given off, which runs upwards and backwards to make a shallow connection with the anterior extremity of the sulcus lingualis. Going slightly further forward we find a short forwardly directed branch, and midway between this and the anterior extremity the fissure anastomoses with an elaborately branching segment of the sulcus temporalis inferior (*Ti*).

FRONTAL LOBE.

Principal sulci.—The *precentral sulci* (*prs* and *pri*) form a continuous fissure, the general direction of which is parallel to the sulcus centralis (*c*). Above it just reaches the mesial surface, while below it falls short of the sylvian fissure by 7 or 8 mm. The two elements can easily be distinguished; the upper (*prs*) ends below in a bifurcation, the anterior branch of which joins the sulcus precentralis inferior (*pri*), while the posterior, as has been stated above, makes a superficial connection with the sulcus centralis.

The *sulcus frontalis superior* (*fs*) falls into two segments, of which the posterior (*fs₁*) runs behind into the sulcus precentralis superior. In front it

is carried forwards and inwards so as to overlap the anterior segment for a considerable distance. The anterior segment (fs_2) ends behind in a transverse fissure, which runs right across the gyrus frontalis medius, and probably belongs to the sulcus frontalis medius series.

The *sulcus frontalis medius* (fm) can hardly be distinguished at all as an independent fissure; it is probably represented by four different segments, each of which is in communication with other fissures. There is posteriorly the transverse fissures referred to above; then come two other elements (fm_2 and fm_3) running in the same direction and joining the sulcus frontalis inferior below, and anteriorly a short sagittal fissure (fm_4) connected on the one hand with the sulcus frontalis superior and on the other with the sulcus fronto-marginalis (fma).

The *sulcus frontalis inferior* (fi) is a straight clearly defined sulcus continuous behind with the sulcus precentralis inferior (pri), and near its anterior end with the sulcus radiatus (r). It is broken at about the middle of its length by a deep annectant gyrus. Its connections with the sulcus frontalis medius have already been referred to. Below it gives off, between the sulcus diagonalis (d) and the ramus anterior ascendens (ra) of the sylvian fissure, a well developed branch ($fi a$) which runs downwards, at the same time bending forwards, and appears to join the sylvian fissure, though in reality not continuous with it.

The *sulcus cinguli* (sc) is a continuous fissure without peculiarities.

Gyri and smaller sulci.—The *gyrus centralis anterior* varies from 10 to 20 mm. in width. It is almost completely separated from the other convolutions on the lateral aspect of the frontal lobe, and is cut across in the middle by a branch of the sulcus precentralis superior. Near its upper end it is indented by a small triangular fissure, the posterior limit of which apparently joins the sulcus centralis (c).

The *lobulus paracentralis* is bounded in front by a well-marked branch of the sulcus cinguli (sc), which almost reaches the supermesial border. It measures about 30 mm. in length along the upper boundary. A small tridiate fissure situated in it forms a compensating arc in reference to the end of the sulcus centralis.

The *gyrus frontalis superior* on the mesial surface measures some 28 mm. across near its posterior end. It becomes narrower as it passes forwards till in the neighbourhood of the frontal pole its width is reduced to 18 mm.; it then broadens out again slightly. Numerous fairly deep sulci, some independent others connected with the sulcus cinguli, break up its surface, and conspicuous among them is the *sulcus rostralis* (rts), a straight fissure 38 mm. in length terminating at each end in a bifurcation.

On the lateral surface the gyrus is also a broad one, particularly near its anterior end, where it measures 25 mm. across. Its surface is also much indented either by branches of the sulcus frontalis superior (*fs*) or by the segments of the *sulcus frontalis mesialis* (*fms*).

The *gyrus frontalis medius* measures about 30 mm. across, and is divided up by fissures which have already been described.

The *gyrus frontalis inferior* occupies a smaller area than the other gyri on the lateral surface. The *pars basilaris* is traversed by a well-developed *sulcus diagonalis* (*d*), which joins the sylvian fissure below and ends above in the angle included between *fi* and *pri*. In front of *d*, and in a general way parallel to it, is the downwardly directed branch of the sulcus frontalis inferior (*fia*). There is a fairly large *pars triangularis*, which is rather more square than triangular, and is cut partially into two portions by the *sulcus radiatus* (*r*).

The *orbital surface* contains the usual straight *sulcus olfactorius*, and a rather elaborate and irregular series of fissures representing the *sulcus orbitalis* (*orb*). An H-shaped element can be distinguished among these, the outer limit of which lies near the orbitolateral border.

PARIETAL OCCIPITAL AND TEMPORAL LOBES.

Principal sulci.—The *sulcus postcentralis inferior* (*poi*) is separated from the sulcus postcentralis superior (*pos*). Below it is connected with the sylvian fissure by the sulcus subcentralis posterior (*scp*), from which it is incompletely separated by a deep annectant gyrus. 26 mm. from the sylvian fissure it ends in a transverse member about 25 mm. in length.

The *sulcus postcentralis superior* (*pos*) is of about the same length as *poi*. It ends both above and below in transverse pieces. The upper one forms posteriorly a very shallow connection with the sulcus parietalis superior (*ps*), while the lower one joins the sulcus interparietalis (*ip*). There is also another connection with latter between the two.

The *sulcus interparietalis* (*ip*) at its lower and forward extremity ends freely in front of the ramus posterior ascendens of the sylvian fissure; it then runs upwards for about 30 mm., anastomosing in two places with the sulcus postcentralis superior (*pos*); then, turning slightly more towards the occipital pole, it gives off on one side the sulcus intermedius primus (*ima*), and on the other an inwardly directed branch (*ipm*). It then runs backwards horizontally for 37 mm. to join the sulcus transversus occipitalis (*tr*). A deep annectant gyrus separates the posterior segment (*ip₂*), to which the mesial branch (*ipm*) belongs, from the anterior segment (*ip₁*). The inner limb of *tr* is connected with the sulcus occipitalis paramesialis. About 15 mm. behind the former, and running on the whole in a direction parallel to it, is fissure

which may probably be identified as the *sulcus lunatus* (*lun*). It is a well marked fissure measuring about 33 mm. from end to end, traversed in the middle by a deep annectant gyrus and connected with *tr* by a sulcus, which has the appearance of being a continuation of *ip*. Its most anterior point lies some 25 mm. from the occipital pole. The stria of Gennari extends to within 8 mm. of its lip.

The *sulcus temporalis superior* (*Ts*) has the appearance of being a continuous fissure, but is, in reality, an annectant gyrus which rises almost to the surface and separates off a short anterior H-shaped portion. Behind this, the main fissure, runs a more or less typical course; it gives off short side branches and behind the end of the sylvian fissure turns upwards to form a ramus ascendens (*Tsa*) which ends above in a bifurcation. At the bend it is fused for a short distance with a segment of the *sulcus temporalis medius* (*Tm*).

The *sulcus temporalis medius* (*Tm*) is as usual separated into numerous irregular segments. The one referred to above may be reckoned as the fourth. After leaving *Ts* it runs sagittally backwards and joins the lower part of the *sulcus lunatus*. It may perhaps be considered to have risen from the junction of the *sulcus occipitalis lateralis* (*ol*) with a part of *Tm*.

The *sulcus temporalis inferior* (*Ti*) is very irregular.

Gyri and smaller sulci.—The gyrus centralis posterior is rather irregular in form owing to the fact that it is cut into by the upper and the lower extremities of the *sulcus postcentralis superior* and the upper extremity of the *sulcus postcentralis inferior*. The union of the latter fissure with the sylvian by means of the *sulcus subcentralis posterior* completely separates the lower part of the convolution from the gyrus supramarginalis.

The *praecuneus* measures 32 mm. along its upper border. On its surface may be seen the inner end of the *sulcus parietalis superior* (*ps*), the *sulcus subparietalis* (*sp*) and the *sulcus praecuneus* (*pc*). The latter is a gently curved fissure running upwards and slightly forwards, which ends below in a bifurcation continuous with the fossa parieto-occipitalis. The *sulcus subparietalis* (*sp*) consists of an upper and a lower portion connected by a short vertical segment. The upper portion forms a compensating arc round the end of the *sulcus parietalis superior*, while the lower portion is superficially continuous in front with the *sulcus cinguli* (*sc*).

The *lobulus parietalis superior* forms an area about 60 mm. long by about 23 mm. wide. The three gyri arcuati, of which it is typically composed, are difficult to define with certainty. The *sulcus parietalis superior* (*ps*) separates off an anterior area which forms a U-shaped convolution round the end of the *sulcus cinguli* (*sc*), bounded laterally by the upper transverse member of the *sulcus postcentralis superior* (*pos*). *ps* itself is a deep conspicuous

fissure, about 40 mm. long, running inwards and slightly backwards. It is continued over into the praecuneus, where it ends in a small bifurcation. Behind *ps* is a straight strip about 10 mm. broad, bounded posterior by the sulcus interparietalis, and then comes a rectangular area delimited at the occipital end by the sulcus transversus occipitalis. This may be taken to represent the gyrus arcuatus posterior; it contains the lateral end of the fossa parieto-occipitalis (*fpo*), and two small independent fissures, one in front and one behind.

In the *lobulus parietalis inferior* the *gyrus supramarginalis* can be clearly distinguished. It is bounded in front by the lower part of the sulcus interparietalis (*ip*), and behind by the sulcus intermedius primus (*ima*). Both its anterior and its posterior limbs are rather more than 10 mm. wide. Above it is prolonged into a backwardly projecting tongue.

The *gyrus angularis* consists of a broad triangular area lying above, which is marked by one or two shallow grooves, and of two short limbs which stretch downwards on either side of the ramus ascendens of the sulcus temporalis inferior (*Tsa*). The *sulcus intermedius secundus* (*imp*), an insignificant oblique fissure about 15 mm. long, forms part of the boundary of the upper area.

The *cuneus* is rather large and has the typical triangular form. It contains lying parallel to the sulcus retrocalcarinus (*im*) about 4 mm. above it, the *sulcus cunei* (*lss*), a straight fissure 22 mm. long giving off a short vertical branch. 12 mm. above that again may be found the *sulcus occipitalis paramesialis* (*o prm*). The latter is a slightly curved fissure running parallel to the supermesial border and giving off a branch which runs outwards on to the lateral surface and joins the sulcus transversus occipitalis (*tr*).

The *gyrus temporalis superior* on its upper surface is raised up into two broad transverse gyri of Heschl. The boundaries of these are indicated on the lateral surface by the two sulci temporalis transversi (*T. tr*), and by the ramus posterior descendens (*rpd*) of the sylvian fissure. The breadth of the lateral surface of the gyrus is from 12 to 16 mm.

In the *gyrus lingualis* is a well developed *sulcus lingualis* (*lsi*), the upper lip of which is strongly operculated. It forms the lower boundary of the striate area.

RIGHT HEMISPHERE.

FISSURES SEPARATING LOBES OF THE HEMISPHERE.

The *sylvian fissure* (*Fsy*).—The *ramus anterior ascendens* (*ra*), into which the lower end of the sulcus diagonalis (*d*) opens, is very short and joins the main stem about 10 mm. behind the *ramus anterior horizontalis* (*rh*); 45 mm. behind this the fissure forks into the *rami posteriores ascendens* and *descendens* (*rpa* and *rpd*), each about 13 mm. length and directed rather abruptly upwards and downwards. A shallow connecting sulcus, running between the

two posterior branches continues the direction of the main fissure, and opens behind into the sulcus temporalis superior. The two sulci subcentrales (*sca* and *scp*) are both strongly developed and form deep junctions with the sylvian fissure.

The *sulcus centralis* (*c*) cuts the supramesial border above and below and falls short of the sylvian fissure by about 6 mm. Its anterior wall is raised up into three well marked gyri, interlocking with three corresponding gyri on the posterior wall. On each side the two lower gyri are larger than the upper one, and their positions are clearly indicated in the lateral surface by the configuration of the fissure. Two small forwardly directed branches further mark the position of the middle gyrus on the anterior wall.

The *fossa parieto-occipitalis* (*fpo*) is practically the same as in the left hemisphere.

The *sulcus calcarinus* (*cal*) is also much the same as in the left hemisphere. The terminal bifurcation on the lateral surface is not quite so conspicuous.

The *sulcus collateralis* (*col*), near its anterior end is joined by the *sulcus rhinencephali inferior* (*sri*). As in the left hemisphere it runs backwards, maintaining its continuity till it ends behind in the sulcus lingualis (*lsi*). It is, however, partially separated from the latter fissure by a deep annectant gyrus. A short way in front of this it gives off an outwardly directed branch (*col a*), and in front of this again is joined by a fissure (*col b*) which almost exactly corresponds in its direction and degree of development with one described in the left hemisphere as making a shallow connection with the anterior end of the sulcus lingualis (*lsi*). In this case *lsi* does not run so far forward and thus falls short of it.

FRONTAL LOBE.

Principal fissures.—The *sulcus precentralis inferior* (*pri*) at the lower end is connected with the sylvian fissure by means of the sulcus subcentralis anterior (*sca*). From its lower end it runs straight upwards for 28 mm. to the point at which the sulcus frontalis inferior (*fi*) is given off; it then turns slightly in a posterior direction, and after running for 13 mm. ends above in a bifurcation which arches round the lower end of the sulcus precentralis superior (*prs*).

The *sulcus precentralis superior* (*prs*) is about 32 mm. in length; the posterior segment of the sulcus frontalis superior (*fs₁*) joins it near the middle. A curved *sulcus precentralis marginalis* (*marg*) lies on the lateral surface above the inner end of *prs*, while on the mesial surface a *sulcus precentralis mediales* (*pr med*) can be distinguished. These two fissures form a shallow connection across the supermesial border.

The *sulcus frontalis superior* (*fs*) falls into two segments. The posterior of these (*fs*₁) consists of a straight portion about 19 mm. in length, which ends in front in a conspicuous bifurcation. The anterior (*fs*₂) is much longer reaching forward almost as far as the frontal pole, where it joins the sulcus frontomarginalis (*fma*). It ends behind in a vertical member (*fm*₁), 30 mm. long, cutting almost completely across the gyrus frontalis medius. As is suggested for the corresponding element in the left hemisphere, this may possibly be more correctly identified as a part of the sulcus frontalis medius.

The *sulcus frontalis medius* (*fm*), in addition to the piece referred to, consists of a sinuous fissure (*fm*₂), roughly longitudinal in direction, lying in the more anterior part of the gyrus frontalis medius. Connected at one point with the sulcus radiatus (*r*), it ends behind in a transverse segment, and in front it joins a fissure of considerable length (*x*), the upper end of which is united with *fs*, while below it falls within the pars triangularis running parallel to *r*.

The *sulcus frontalis inferior* (*fi*) is a deep horizontal fissure 28 mm. in length, completely connected behind with the sulcus precentralis inferior (*pri*) and in front with the *sulcus radiatus* (*r*).

The *sulcus frontomarginalis* (*fma*) is represented by three sulci, of which the inner one is joined by *fs*.

The *sulcus cinguli* (*sc*) is a continuous fissure with the peculiarity that it ends in front opposite the lower border of the genu of the corpus callosum.

Gyri and smaller sulci.—The *gyrus centralis anterior* presents no special features. It is almost shut off from the two upper horizontal gyri of the lateral surface, and completely separated from the lower one. It is rather narrow, varying in width from 10 to 15 mm.

The *lobulus paracentralis* and the mesial portion of the *gyrus frontalis superior* form a continuous strip about 25 mm. wide, but becoming somewhat narrower towards the frontal pole. Into this run four upward branches from the sulcus cinguli, while its surface is broken by one or two independent fissures and the sulci rostrales. The upper of these *rts* is 46 mm. long, and the narrow isthmus which separates it from the sulcus centralis is slightly below the general surface. The lower one, *rti*, is a straight fissure measuring 37 mm. from end to end.

The gyrus frontalis superior in the lateral surface varies from 20 to 30 mm. in breadth. The *sulcus frontalis mesialis* (*fms*) forms a conspicuous series of depressions in its surface.

The *gyrus frontalis medius* is about 30 mm. in breadth posteriorly and narrows somewhat in front. Its fissures have already been described.

The *gyrus frontalis inferior*. The pars basilaris is incompletely separated from the pars triangularis. The sulcus diagonalis (*d*) is a straight upwardly

directed fissure 18 mm. in length, connected below with the ramus anterior ascendens of the sylvian fissure. It lies some 7 or 8 mm. in front of the sulcus frontalis inferior (*fi*). The pars triangularis is completely divided right up to its apex by the sulcus radiatus (*r*), in front of which lies the long fissure (*x*) referred to in describing the sulcus frontalis medius (*fm*).

The *orbital surface* has essentially the same conformation as in the left hemisphere.

PARIETAL, OCCIPITAL AND TEMPORAL LOBES.

Principal sulci.—The *sulcus postcentralis inferior* (*poi*) is rather unusual in that its lower end lies behind the ramus posterior ascendens (*rpa*) of the sylvian fissure opposite the point at which the descending branch is given off. From that position *poi* runs upwards, bending slightly forwards for 27 mm., then joins a horizontal cross-piece, the anterior end of which makes a shallow connection with the sulcus centralis, while its posterior end is connected over a narrow slightly sunk gyrus with the sulcus postcentralis superior (*pos*).

The *sulcus postcentralis superior* (*pos*) consists of a more or less straight middle piece running upwards and downwards, which ends above in a short cross-piece, and below in a much longer one. The latter is produced forwards almost across the gyrus centralis posterior, and backwards to branch again, and form connections on the one hand with the sulcus postcentralis inferior (*poi*), and on the other with the sulcus interparietalis (*ip*).

The *sulcus interparietalis* (*ip*) consists of two quite distinct segments. The anterior of these (*ip*) is a short oblique fissure bifurcated at each end. The lower posterior branch makes the connection with *pos* already referred to, and is joined over a deep annectant gyrus by the ramus ascendens of the sulcus temporalis superior (*Tsa*). The posterior segment *ip₂* consists of a portion 35 mm. long, which runs roughly parallel to the superomesial border and ends behind in the sulcus transversus occipitalis (*tr*). In front it sends off a conspicuous inward branch (*ipm*) 23 mm. long, and also an outer one which is slightly shorter and directed forwards.

The *sulcus temporalis superior* (*Ts*) is a conspicuous fissure ending above in a superficial junction with *ip*. It is also connected with the sylvian fissure, and in two places with the sulcus temporalis medius (*Tm*). A sulcus temporalis transversus superior runs obliquely across in front of its anterior end.

The *sulcus temporalis medius* (*Tm*) consists posteriorly of a long segment (*Tm₁*), made up of a well defined ramus ascendens, which is continued downwards and forwards to end in a bifurcation. The anterior branch runs forwards and slightly upwards and joins *Ts*. The second connection with *Ts* lies just posterior to this. In front three more segments may be distinguished

forming a fairly regular line of fissures. The anterior of these (Tm_1), which is straight, and the second (Tm_2), which is H-shaped, are the largest.

The *sulcus temporalis inferior* (Ti) is also a conspicuous and fairly regular fissure. It consists of two segments, the anterior being bifid at each end, and the posterior a long fissure joining Tm_2 in front and the sulcus lingualis (lsi) behind.

Gyri and smaller sulci.—The *gyrus centralis posterior* is very narrow near its upper end, measuring only about 7 mm. across, but widens out considerably below where it fuses with the *gyrus supramarginalis*. This region is separated off by the junction of the sulcus postcentralis inferior with the sulcus centralis. It contains a deep and well developed *sulcus subcentralis posterior* (scp), ending above in a cross-piece, and posterior to that a short obliquely placed fissure.

The *praecuneus* bears a strong resemblance to that of the left hemisphere, but covers a larger area, measuring 42 mm. along its upper border. At its posterior end a *sulcus praecunei* (pc) may be found which joins the fossa parieto-occipitalis (fpo) at its slower extremity; running forwards and upwards from that point it crosses over on to the latter surface, where it ends in a bifurcation. The *sulcus subparietalis* (sp) is a conspicuous H-shaped fissure, of which the long anterior ascending limb ought possibly to be regarded as a sulcus praecunei. In front of it are two small independent sulci.

The *lobulus parietalis superior* consists of a well defined *gyrus arcuatus posterior* and an irregular anterior portion. The latter contains the *sulcus parietalis superior* (ps), an oblique fissure 14 mm. long branching at each end and the upper extremity of the sulcus praecunei (pc). The former is a rectangular area averaging about 35 mm. in length and 27 mm. in breadth; it is bounded in front by median branch of the sulcus interparietalis (ipm), and behind by the sulcus transversus occipitalis (tr). It contains the upper end of the fossa parieto-occipitalis, and behind that a sigmoidally-shaped sulcus, which forms a superficial connection with the sulcus occipitalis paramesialis ($o prm$).

In the *lobulus parietalis inferior*, owing to the shortness of the ramus posterior ascendens (rpa) of the sylvian fissure, the *gyrus supramarginalis* is small, and it is not easy to assign definite boundaries to it. The *gyrus angularis* on the other hand is large and is bounded very clearly behind by the *sulcus intermedius primus* (ima), an independent fissure about 45 mm. long, running parallel to the ramus ascendens of the sulcus temporalis superior (Tsa) about 15 mm. behind it. In the *gyrus parietalis inferior posterior* may be found the ramus ascendens of the sulcus temporalis medius (Tm), and a longitudinally disposed fissure (ol), measuring 30 mm. from end to end, which runs backwards towards the occipital pole, and may perhaps be identified as the *sulcus occipitalis lateralis*.

In the *occipital area* on the lateral surface of the hemisphere may be found two parallel fissures which run upwards and slightly forwards, about 5 or 6 mm. apart. The striate area extends to the lip of the posterior of these, which may therefore be regarded as the *sulcus lunatus (lun)*. It is about 25 mm. long, and in the middle it is approximately 15 mm. from the occipital pole. The anterior fissure of the two stretches round on to the tentorial surface and almost joins the sulcus temporalis inferior. It may perhaps be identified as the *sulcus polaris inferior (pol i)*.

The *cuneus* presents no unusual features; it contains a rather short *sulcus cunei (lss)* and a well developed *sulcus occipitalis paramesialis (o prm)*. Below the retrocalcarine fissure is the *sulcus lingualis (lsi)*, the arrangement of which is much the same as in the left hemisphere, except that it does not extend so far back.

The *gyrus temporalis superior* is about 14 mm. in width. On its upper surface are two transverse gyri of Heschl, which are not quite so well developed as those of the left hemisphere.

The *gyrus temporalis medius* measures about 18 mm. in breadth.

DESCRIPTION OF FIGURES.

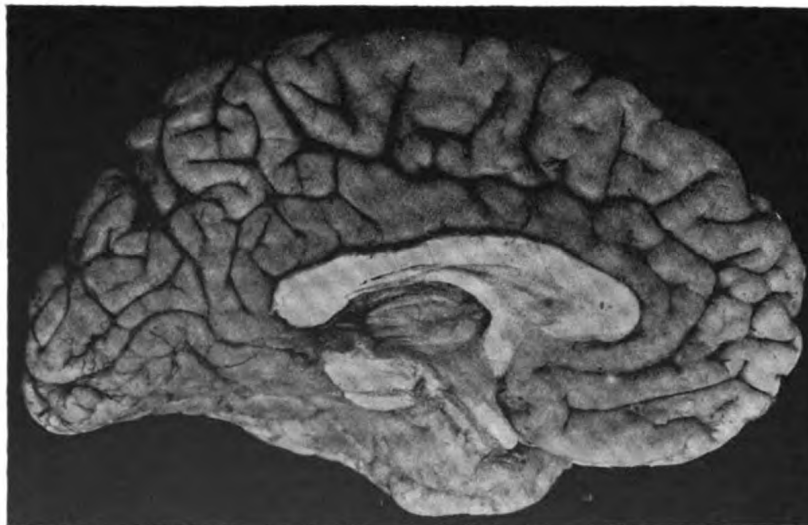
- IA. Left hemisphere, lateral surface: Photograph; 1B. Left hemisphere, lateral surface: Key.
 IIA. Left hemisphere, mesial surface: Photograph; IIB. Left hemisphere, mesial surface: Key.
 IIIA. Both hemispheres, from above: Photograph; IIIB. Both hemispheres, from above: Key.
 IVA. Both hemispheres, from below: Photograph; IVB. Both hemispheres from below: Key.
 VA. Right hemisphere, lateral surface: Photograph; VB. Right hemisphere, lateral surface: Key.
 VIA. Right hemisphere, mesial surface: Photograph; VIB. Right hemisphere, mesial surface: Key.

LIST OF ABBREVIATIONS USED IN FIGURES AND SOMETIMES IN TEXT.

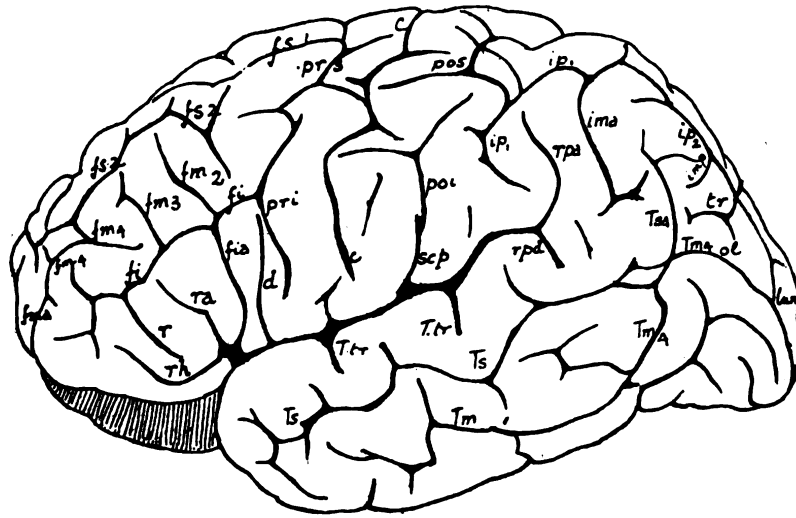
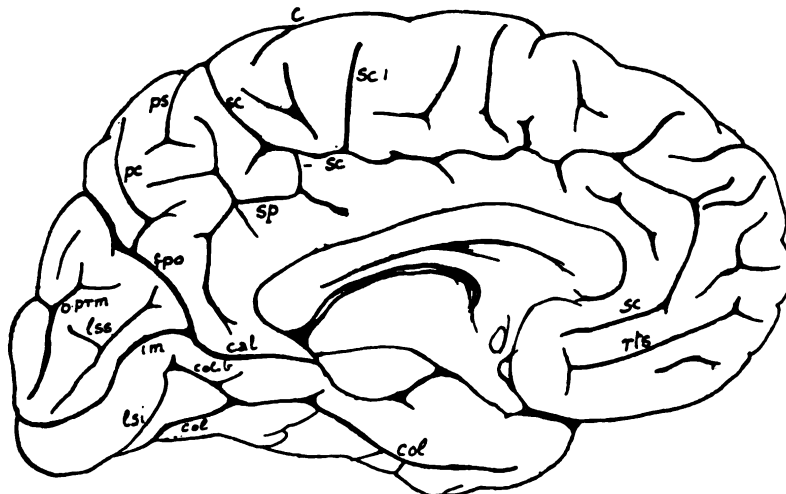
Fissura sylvii	Fsy	Sulcus orbitalis	orb
Ramus posterior ascendens	rpa	Sulcus postcentralis superior	pos
Ramus posterior descendens	rpd	Sulcus postcentralis inferior	poi
Ramus anterior ascendens	ra	Sulcus subcentralis posterior	scp
Ramus anterior horizontalis	rh	Sulcus interparietalis proprius	ip
Sulcus centralis	c	Sulcus occipitalis transversus	tr
Fossa parieto-occipitalis	fpo	Sulcus parietalis superior	ps
Sulcus calcarinus	cal	Sulcus intermedius primus	ima
Fissura collateralis	col	Sulcus intermedius secundus	imp
Branches of f. collateralis	col a and col b		Sulcus subparietalis	sp
Sulcus precentralis superior	prs	Sulcus praecuneus	pc
Sulcus precentralis inferior	pri	Sulcus temporal superior	Ts
Sulcus precentralis marginalis	marg	ramus ascendens	Tsa
Sulcus precentralis medialis	pr med	Sulcus temporalis transversus	T tr
Sulcus frontalis superior	fs	Sulcus temporalis medius	Tm
Sulcus frontalis inferior	fi	Sulcus temporalis inferior	Ti
Sulcus frontomarginalis	fma	Sulcus rhinencephali inferior	sri
Sulcus radiatus	r	Sulcus lingualis	lsi
Sulcus diagonalis	d	Sulcus retrocalcarinus	im
(For description of x vide text.)			Sulcus cunei	lss
Sulcus subcentralis anterior	sca	Sulcus polaris inferior	pol i
Sulcus cinguli	sc	Sulcus lunatus....	l
Sulcus rostralis superior	rts	Sulcus occipitalis lateralis	ol
Sulcus rostralis inferior	rti	Sulcus occipitalis paramesialis	o prm



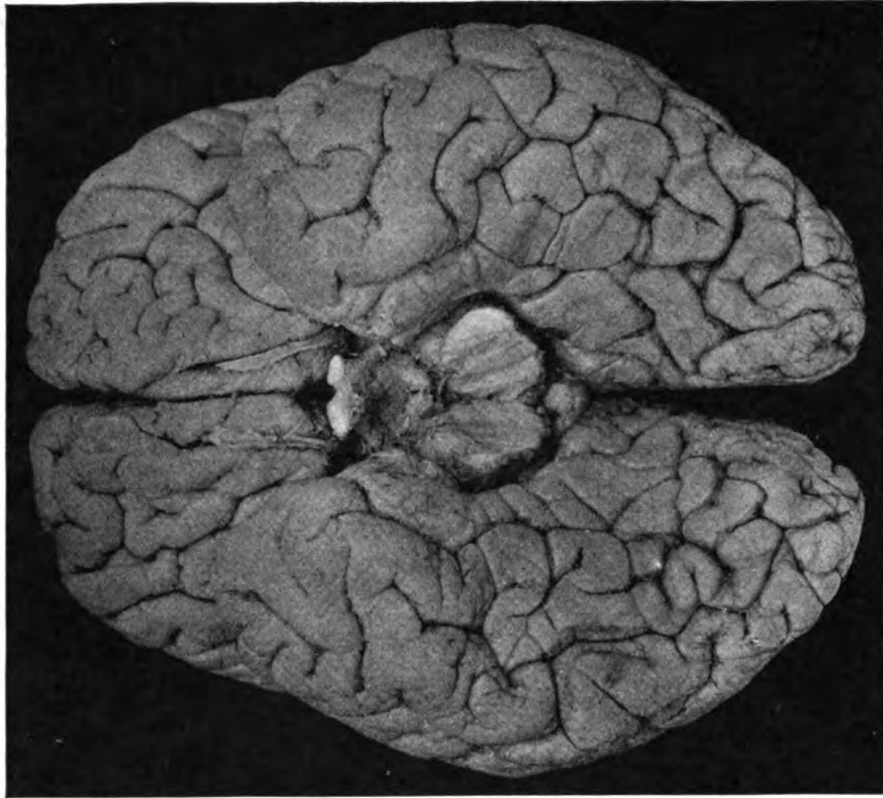
Ia.



IIa.

**IB.**

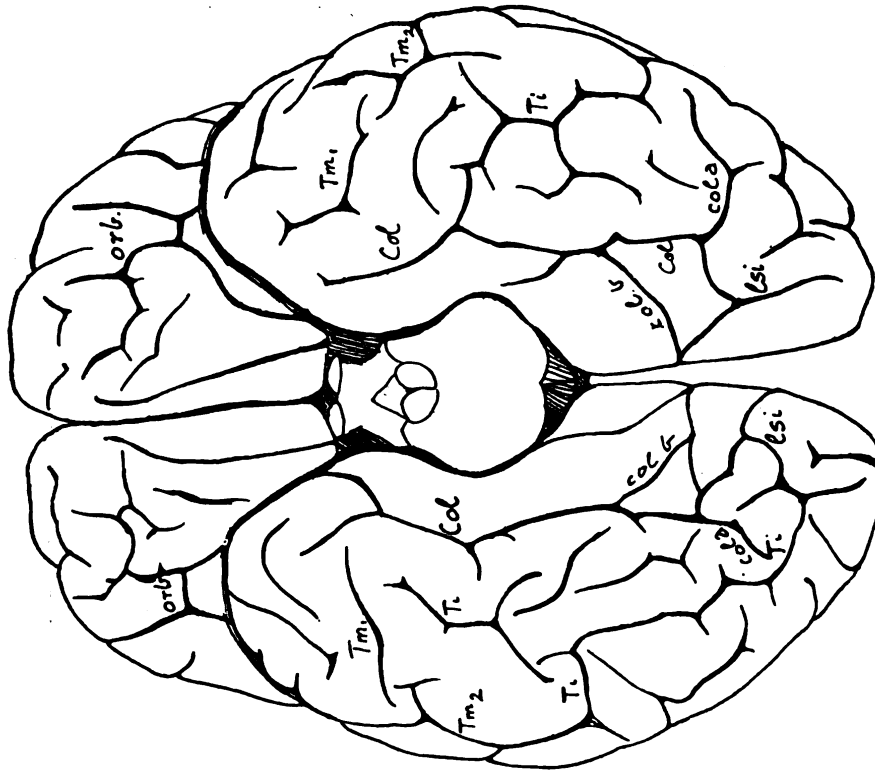
II B.



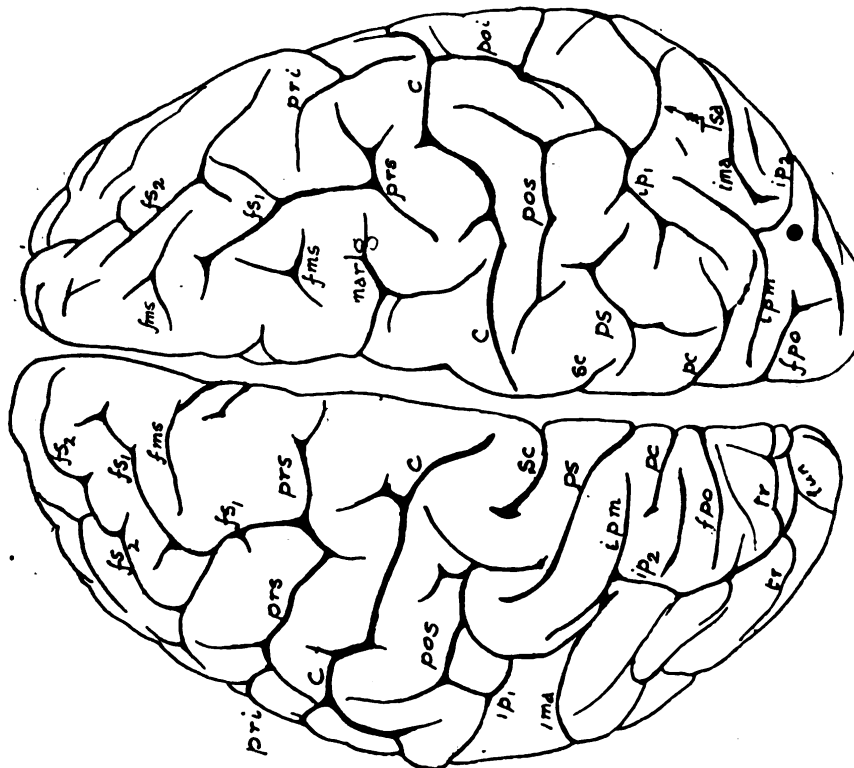
IVa.



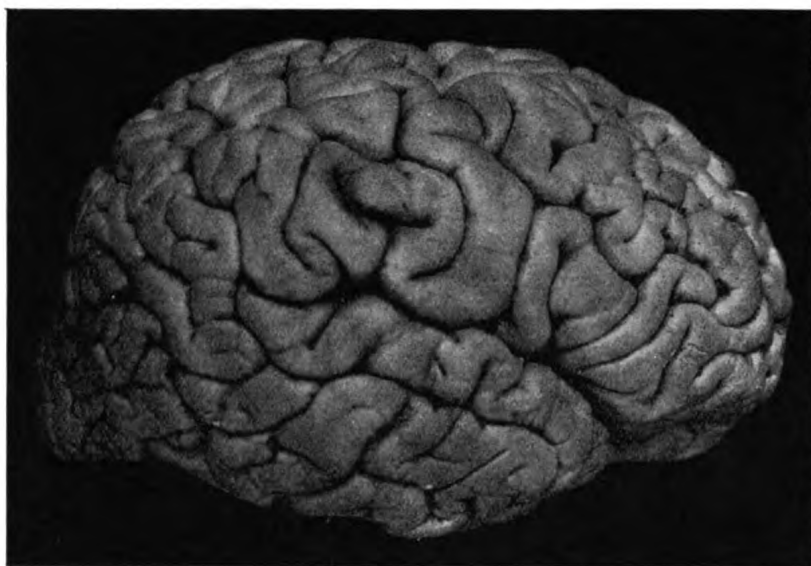
IIIa.



IVB.



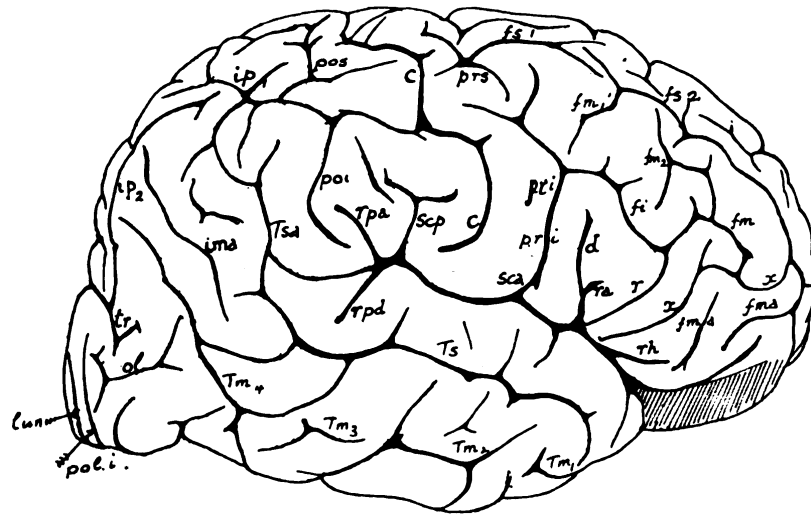
III.B.



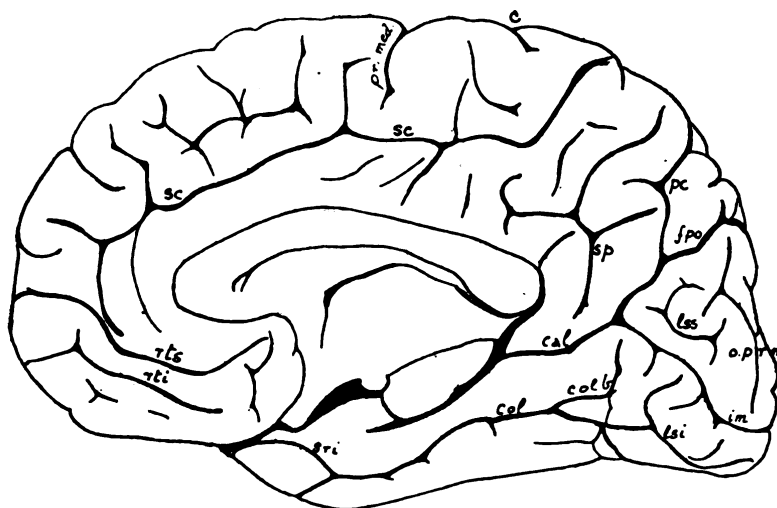
VA.



VIA.



V.B.



VI.B.

A Note on Calcification in Cerebral Neoplasms.

By LEWIS H. WEED, M.D.

[From the Pathological Laboratory of the London County Asylums.]

The frequency of occurrence and the histological characteristics of the various deposits of calcium met with so often in cerebral neoplasms have been the objects of this study. So far as can be ascertained, no statistical tables regarding these calcified masses have been published, although the text books dealing with cranial new growths mention their frequent occurrence, especially in endotheliomata. No attempt also has in the past been made to classify the various forms in which the lime salts are laid down, and it is hoped that the classification here suggested will prove of service in the ultimate solution of the problems centreing about the deposition of calcium in cerebral neoplasms.

This study has been based on 55 cases of cerebral neoplasms which have been met with in the routine examinations made in the Pathological Laboratory of the London County Asylums at Claybury. All of the cases represent true new growths, the tuberculomata and the syphilomata being excluded from the tables. In most cases the diagnosis of a calcified deposition has been based on the characteristic staining reactions of calcium to hæmatoxylin. This diagnosis has been confirmed by chemical diagnosis in those few cases in which sufficient lime salts were present to permit a qualitative test. The neoplasms have been classified according to the official diagnosis made in the Pathological Laboratory on each case, as it was felt that in this way uniformity in terminology and in classification would obtain.

In the 55 cases studied, it was found that calcium deposits could be identified with certainty in 22 of the cases (40 per cent.). Analysis of the different types of tumour shows that this percentage holds very constant throughout the true cerebral neoplasms, *i.e.*, those which arise from structures

included within the pachymeninges. Thus, calcium salts are met with in 43·8 per cent. of the cases diagnosed as endotheliomata, and in 44·4 per cent. of the cases classified as fibro-endotheliomata. Combining these two under one great division of endotheliomata, the percentage of those containing calcium deposits becomes 44·0. This class of tumour constitutes slightly less than half of the total number of cases. Of the gliomata and gliosarcomata, one-third of those investigated contain definite masses of lime salts, while in the other varieties of sarcomata the percentage rises to 37·5. The two classes constitute about one-third of all the neoplasms. Four cases of intracranial adenomata occur in this series of tumours—three arising apparently from the hypophysis cerebri and one from the plexus choroidea of the third ventricle. In these growths, calcium is found in three of the four. Great contrast to this frequency of occurrence of calcium deposits is offered by the six cases of metastatic neoplasm in this series. Four of these growths were secondary carcinomata, the fifth a chondroma, and the sixth a lipoma. In none of these tumours was calcium found in any form. Following are the findings in tabular form :—

Classification of Neoplasm.	Number of Cases.	Per Cent. of Total Series.	Number containing Calcium.	Per Cent. containing Calcium.
Endotheliomata	16	29·1	7	43·8
Fibro-endotheliomata	9	16·4	4	44·4
Both varieties of endotheliomata	25	45·4	11	44·0
Gliomata	6	10·9	2	33·3
Gliosarcomata	3	5·5	1	33·3
Gliomata and gliosarcomata	9	16·4	3	33·3
Sarcomata (including gliosarcomata)	11	20·0	4	36·4
Sarcomata (excluding gliosarcomata)	8	14·6	3	37·5
Secondary carcinomata	4	7·3	0	0
Adenomata	4	7·3	3	75·0
Cyst of the third ventricle	1	1·8	0	0
Lipoma	1	1·8	0	0
Chondroma	1	1·8	0	0
Fibroma of the ventricular choroid	1	1·8	1	100·0
Growth in lateral ventricle*	1	1·8	1	100·0
Totals	55	100·0	22	40·0

* No diagnosis has been made of the nature of this growth, which represents one of a series of small rounded elevations in the wall of the lateral ventricle. The whole hemisphere shows an extreme grade of neurogliosis. Microscopically, the elevations consist of a loose reticular structure, apparently neuroglial in character, with many calcified bodies in it. These depositions represent undoubtedly old vascular channels, completely replaced by the lime salts. In addition to these tubular masses of calcium are many punctate masses of calcium.

Systematic examination of the different calcium deposits in this series of 55 cerebral neoplasms has led to the following classification of the morphology of the calcified bodies :—

(1.) *Punctate*.—Under this heading are included the commonest forms in which calcium is met with. On microscopic section, they appear as small circular bodies, at times quite irregularly outlined, showing the characteristic staining reaction. Two forms of these punctate bodies are found :—

- (a) *Psammoma* bodies, in which there is no apparent internal structure to the mass, the external circular form being characteristic.
- (b) *Corpora amylacea*, in which the characteristic concentric rings, simulating the starch granules, are made out.

(2.) *Vascular*.—This class includes those deposits of calcium which by their morphology represent the replacement of a whole vascular channel by the lime deposition. On microscopic examination, they show the solid cord-like appearance of an occluded vessel, branching forms being frequently encountered.

(3.) *Trabecular*.—This variety comprises those irregular, plate-like collections of lime salts which are found in the fibrous trabeculae of the various neoplasms which have a fibrous framework. The deposit may be a very small spicule occurring in the interstices of the trabecula or it may be a large plaque displacing the fibrous strands.

(4.) *Amorphous*.—Included in this subdivision are those deposits of lime salts which show no characteristic nor constant morphology, but which are really a sort of amorphous calcium debris.

(5.) *Periarterial*.—In this form, the calcium deposit encircles the arteries as a ring, as first described by Beadles,* in a case of telangiectasis of the frontal lobe. In none of the neoplasms examined in this study were such deposits found.

Analysis of the 55 cases of cerebral new-growth for the occurrence of the calcium in the various forms suggested above, has led to the compilation of the following table, in which the percentages of the various morphological forms of calcium have been based on the finding of calcified deposits in 22 cases :—

* Beadles, "Archives of Neurology" (F. W. Mott), Vol. I, page 440.

Classification.	(1) Punctate.				(2) Vascular.		(3) Trabecular.		(4) Amorphous.		(5) Periarterial.	
	Psammoma.		Amylacea.									
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
All varieties containing calcium	15	68.2	5	22.7	4	18.2	4	18.2	6	27.3	0	0
Endotheliomata	5	31.3	4	25.0	1	6.3	2	12.5	1	6.3	0	0
Fibro-endotheliomata	2	22.2	1	11.1	0	0	1	11.1	1	11.1	0	0
Both varieties of endotheliomata	7	28.0	5	20.0	1	4.0	3	12.0	2	8.0	0	0
Gliomata	2	33.3	0	0	1	16.7	1	16.7	1	16.7	0	0
Gliosarcomata	1	33.3	0	0	0	0	0	0	0	0	0	0
Gliomata and gliosarcomata	3	33.3	0	0	1	11.1	1	11.1	1	11.1	0	0
Sarcomata (including gliosarcomata)	3	27.3	0	0	1	9.1	0	0	1	9.1	0	0
Sarcomata (excluding gliosarcomata)	2	25.0	0	0	1	12.5	0	0	1	12.5	0	0
Adenomata	2	50.0	0	0	0	0	0	0	2	50.0	0	0
Fibroma	1	100.0	0	0	0	0	0	0	0	0	0	0
Growth in lateral ventricle	1	100.0	0	0	1	100.0	0	0	0	0	0	0

The preceding table shows the far more frequent occurrence of the punctate forms of calcium than of the more complex varieties. It points out also that the punctate psammoma bodies occur about three times as frequently as the corpora amylacea. The punctate psammoma bodies also maintain a high degree of frequency in all the calcium-containing tumours and are not found absent from any of the classes of tumours which contain deposits of lime salts. On the other hand, in this series, the corpora amylacea are met with only in the great inclusive class of endotheliomata and are apparently more common in the pure endotheliomata than in the fibro-endotheliomata. This absence of the corpora amylacea from the glial and adenomatous types of tumours may be significant, but, unfortunately, the numbers of the neoplasms dealt with are too small to enable one to draw definite conclusions.

Of the 22 neoplasms containing calcium, nine cases contain these lime salts in more than one form. The most frequent combination is that of the punctate psammoma bodies with the vascular or trabecular deposits. The two forms of punctate deposits are met with together in only two cases—a rather noticeable fact in view of their great frequency in association with other forms. One neoplasm, a dural endothelioma, contained an enormous amount of calcium; all forms except the vascular and periarterial types were represented.

It is quite impossible from this study to draw conclusions as to the real significance of calcium salts in cerebral neoplasms. The slightly greater frequency with which the lime deposits in one form and other are met with in endotheliomata than in the glial tumours accords with the old deduction that the depositions occur more frequently in the old, slowly growing tumours. The occurrence of calcium masses in 40 per cent. of an unselected series of cerebral neoplasms is quite striking, and the absence of calcium in the metastatic growths seems equally important.

I wish to acknowledge my indebtedness to Dr. F. W. Mott for his kindness in affording me every facility for the examination of this series of cerebral neoplasms.

Notes on the *Ætiology, Pathology and Clinical Aspects of some Cases of Insanity occurring in the Involutional Period of Life.*

By M. B. BAINES, M.D., B.Ch., Oxon, M.R.C.S., L.R.C.P.

It is proposed in this thesis to submit an analysis of 104 consecutive cases whose first attack of insanity occurred between the ages of 50 and 60 years.

The patients are, or have been, all male inmates of the London County Asylum at Claybury.

The choice of the decade between 50 and 60 was entirely an arbitrary one, for presenile insanity not infrequently occurs between the ages of 40 and 50. But, by excluding patients whose insanity commenced before the age of 50, the inclusion of doubtful cases of general paralysis was largely avoided. On the other hand in persons of advanced age, senile dementia may be almost physiological. Therefore, no case was included whose onset of insanity occurred after the age of 60.

The cases investigated fall into the four groups :—A. 38 cases in which the clinical aspects of the disease have been studied by the writer in the wards of the asylum. B. An analysis of the records of 30 patients who had died in the asylum, taken from Dr. Candler's notes in the post-mortem records of the London County Asylum at Claybury. C. Histological work done by the writer, in the Pathological Laboratory of the London County Asylums, on specimens taken from certain of the post-mortem cases. D. An analysis of the notes in the asylum case books of 36 cases who have left the asylum either recovered or discharged to the care of friends.

When this investigation was begun, it was undertaken purely from an analytical standpoint without prejudice in favour of any particular theory, but later, when it was seen how great the influence of arterial degeneration appeared to be in the production of this type of insanity, some emphasis was given to the study of this particular aspect of the question.

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The investigation was pursued on the following lines :—

1. Clinical aspect : Mental state ; circulatory system ; urinary system ; nervous system.
2. Post-mortem records : Brain and meninges ; heart and coronary arteries ; blood vessels, including the cerebral arteries ; kidneys and renal arteries ; evidence of syphilis.
3. Minute pathology : Brain and meninges ; blood vessels ; glia proliferation ; degeneration of nervous tissues.
4. Family history, for neuropathic taint.
5. Personal history : Occupation ; alcoholism ; syphilis and other infections ; injury.

CLINICAL OBSERVATIONS ON 38 CASES.

Circulatory system. Heart.—There was cardiac hypertrophy in 22 cases out of 37 examined. Such hypertrophy varied considerably in degree, the apex being under the sixth rib and in the mid-clavicular line in 11 cases, and in 11 cases anything from $\frac{1}{2}$ to 3 inches external to the mid-clavicular line. Eleven cases presented no sign of cardiac hypertrophy, and in four instances the heart and heart sounds were completely obscured by emphysema and bronchitis.

An accentuated second aortic sound was almost the rule in the 22 cases with hypertrophy, and in 11 of these the sounds at the apex also were louder and more ringing than is normally the case. In five out of 11 instances in which there was no other sign of cardiac hypertrophy, the aortic valves appeared to close with a louder snap than usual. Possibly a rigid atheromatous ampulla aortæ involving the base of the valves would account for this accentuation. Such a condition of the aorta was common in the post-mortem series (*vide infra*).

Evidence of gross valvular disease was present in 10 patients, including eight cases of mitral regurgitation and two cases of roughening of the aortic valves with probably some narrowing of the aortic ring. Only one patient had aortic regurgitation and in his case there was a history of repeated attacks of rheumatic fever.

Arteries.—The peripheral arteries in nearly every case were to a greater or less degree tortuous and hard. An attempt to determine the blood pressure in certain of these cases did not lead to very satisfactory results. Thirteen of the less truculent patients were selected and sphygmometer readings taken with the large Hill and Barnard's instrument. The lowest systolic reading was 168 and the highest 240, three were between 220 and 230, two just over 200 and the remainder between 180 and 200. It is difficult, however, to satisfy oneself as to the value of such observations when dealing with patients with grossly diseased arteries ; for of the two factors involved,

the blood pressure and the resistance of the vessel wall, the latter in these cases is so great as to overshadow the former. Thus in certain cases with tortuous thickened arteries the sphygmographic readings were very high, whilst the other signs usually associated with continued high blood tension, such as hypertrophy of the left ventricle, increased heart sounds, particularly the second aortic, were wanting and there was also a lack of any evidence of renal disease.

It is recognised (Mott in Clifford Allbutt's "System of Medicine") that tortuous thickened arteries may be associated with either a high or low blood pressure and the writer would suggest that in fairly active individuals with tortuous arteries, the presence or absence of left ventricular hypertrophy and the accentuation or not of the second aortic sound are more reliable indications of the state of the blood tension than any sphygmometer readings can be. In 26 cases the *fundus oculi* was examined in order to ascertain the condition of the retinal arteries. These were found to be apparently healthy in half of the cases, whilst in the remainder tortuosity of a greater or lesser degree was found, the arteries varying in appearance from irregular silvery streaks in three instances down to a slight degree of tortuosity hardly distinguishable from the normal.

Kidneys.—Considering the number of cases with marked degenerative changes of the arteries and in which fairly extensive involvement of the kidneys might not unreasonably be expected, evidence of kidney disease was uncommon. The first morning specimen of urine from 36 patients was examined with the following results :—

Apparently natural	21 cases.
Pus (probably from the bladder or urethra)	2 „
Albumen (apart from the cases with pus)	2 „
(In one a faint trace only.)						
Sugar	1 case.
Casts (after centrifugalisation)	9 cases.
Hyaline	2 „
Granular	3 „
Hyaline and granular	4 „

In only one case were the casts abundant; usually they were found only after some little search.

From these figures one may surmise that only one or two of these patients suffer from extensively damaged kidneys, though, on the other hand, several give evidence that their kidneys are not unaffected and in these it is not improbable that more serious trouble may supervene later.

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Nervous system.—Seven patients presented unequal pupils, and in eight cases the light reflex was markedly sluggish in both eyes, and in two cases in one eye only. In 16 instances the pupil phenomena appeared to be normal, and in three cases any inequality of the pupils or alteration of the light reflex could be explained by the presence of iritic adhesions or of advanced cataract.

There was no definite instance of nystagmus. As stated elsewhere the retinal arteries, as shown by ophthalmoscopic examination, were either more or less tortuous in 13 out of 26 patients examined.

Fine tremors of the hands were almost the rule. In the great majority of cases the deep reflexes, and more especially the knee jerks, were increased, and the biceps, triceps, supinator and ankle jerks were often more glib than is normally the case. The superficial reflexes (abdominal, cremasteric and plantar) were usually brisker than normal and varied in degree, not only in different patients but also, in certain instances, in the same patient from time to time. Thus the abdominal or cremasteric reflex could sometimes be obtained on one or other side only, whereas, if the patient were examined again a week later, both sides might react equally well.

Neither ankle clonus nor Babinski's sign was present in any case except in three, in patients with old hemiplegias, where they would naturally be present.

Mental condition.—Like other insane persons, the subjects of insanity in the involutional period present a complex of mental symptoms of which, at least in the present series, melancholia is by far the most common.

For the moment it will be more convenient to exclude the following :—

8 cases of general paralysis.

2 „ „ epileptic dementia.

3 „ „ post hemiplegic dementia.

1 case of polyneuritic psychosis of Korsakow.

1 „ „ Huntingdon's chorea.

1 „ „ dementia associated with post-operative hernia cerebri.

Of the remaining 88 cases, rather less than a half were investigated by the writer, who is indebted to the clinical notes written by his predecessors at Claybury for the remaining cases.

Of the early symptoms before admission to the asylum not very much as a rule can be learnt. The relatives may give a history that the patient was by disposition cheerful or gloomy, quiet or irritable. Possibly he may have suffered from headaches or nervousness. He may have worried over domestic troubles and have magnified trifling discomforts into calamities. Frequently a history is given that the patient became suspicious and possibly violent. He may have complained that people were talking about him or were trying

to injure him in some way. As will be seen later attempts at homicide or suicide were not infrequent.

When seen later in the asylum the mental state presents as a rule a complex of some or other of the following psychic symptoms :—melancholia, mania, delusional insanity and dementia. In the great majority of cases (68 out of 104) the basis of the mental state was melancholia, though in this category the writer has ventured to include several patients who might be considered to be suffering from mania were it not that their maniacal actions seem to have their *raison d'être* in an underlying basis of restless melancholia.

Simple melancholia without delusions is not common in asylums, as these cases can usually be treated at home and either recover or get worse and then are removed to an asylum. In these cases there is a morbid depression with some clouding of the will power, but the reasoning and auto-critical faculties are still present. For example :—

F. W.—Æt. 50. Marked family taint. Worried over domestic troubles and took to drink. He came to think life was not worth living and attempted suicide by placing himself on a railway line. On admission to the asylum he was mentally unstable and was depressed. His memory, reasoning and auto-critical faculties were apparently unimpaired. He rapidly improved and was discharged recovered after a few weeks' detention.

More usually (in almost all of the present series) the disease is more advanced and the patient has lost the power of rousing himself or being aroused from his painful ideas which now become delusions. Thus delusional insanity with a varying degree of dementia superadded complicates the melancholia.

The patient hears voices talking about him, he may think that detectives or others continually spy on him, that he has committed some great crime, or that poison is placed in his food. He may complain that electricity, galvanism, "the wires," invisible rays or fumes are being played on him, and sexual delusions are common.

Three of these cases had hypochondriacal obsessions, *e.g.*, that their bowels were never opened or that the lungs had been burnt out.

Visual, olfactory and taste hallucinations were not present with the exception of the first of these, and then only in two cases out of 40 that were examined. A still more advanced type of this disease is presented by the victims of stuporose melancholia. Berkley in his book on mental diseases thus describes this condition :—

"The patients are entirely sunk in their own calamities, mute, passive, apparently entirely oblivious of what is transpiring around them, and absolutely without will power to rouse themselves out of their stuporose condition.

. . . . That the stuporose condition is only apparent, not real, is shown

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by the anxious expression, the occasional wrinkling of the forehead and by the occasional wild starts and frantic attempts at self-destruction."

A. H. is an example of this type. Age at first attack 55 years. Sister in Brentwood Asylum. No history of drink. For 13 months he had gradually become morose and suspicious and had developed persecutory delusions. He attempted to strangle himself and also to commit suicide by means of carbohc acid. At the present time he practically never speaks, and is passive and resistive. He will stand or sit in the same position for long periods of time. He believes that voices whisper in his ear and that poison is placed in his food. He eats with great reluctance and then only after coaxing by an insistent attendant.

The delusions are apt to impel their owners to violent actions. A patient may think life to be so gloomy an affair as to wish to be rid of it; or, to escape from the hateful influence of a supposed persecutor, he may attempt either to destroy his enemy or, by himself committing suicide, to place himself for ever beyond his reach.

In 31 cases of this series the patient was suicidal. In 17 cases actual attempts at self-destruction had been made, as by hanging, throat cutting, poison, &c., whilst in 14 other instances the patient had threatened or talked about suicide. Similarly, 9 patients had made determined homicidal attacks on individuals, *e.g.*, by strangling, knife wounds, &c., and 10 others had been described as violent or dangerous.

Mania.—Apart from the subjects of general paralysis the cases of mania in which there can be no lingering doubt that the basis of disorder is in reality a state of restless melancholia do not appear to be very common. Only two cases presented this type, and these were both patients with a history of alcoholic excess :—

C. H.—Age at onset 52. A commercial traveller. Grandiose and boastful. He imagines himself to be intimate with the King, declares himself to be *Lux Mundi* and "King of Kings." Certain physical signs suggestive of general paralysis are present. Pupils sluggish to light; tremors of face; increased knee jerks, speech shaky; and he might be considered as a victim of this disease were it not for the fact that the Wassermann reaction both to the blood and cerebrospinal fluid is negative.

H. P.—According to the notes was noisy, restless, grandiose and confused. The pupils were almost inactive to light. Knee jerks brisk, speech shaky. Visual and aural hallucinations were present and the patient was disorientated. There was albumen in the urine. This patient was considered to be probably a case of general paralysis, but the brain was subsequently microscopied and found to be not affected with general paralysis. There was generalised arteriosclerosis, especially of the renal and cerebral arteries.

These cases illustrate the difficulty in certain instances of diagnosing between alcoholic insanity with or without arterio-sclerosis on the one hand and general paralysis on the other.

Dementia.—Some degree of dementia is usually present, and as the disease advances this symptom by replacing the earlier melancholy and delusional states tends to dominate the picture. The memory becomes impaired, especially for recent events, mental reaction may be slow and the intellectual faculties dull, and towards the end dementia may be profound, though rarely so pronounced as in the terminal stages of paretic dementia.

Recovery occurred in rather less than a third of the series, but in a few cases the patient has returned relapsed, and doubtless not a few of the remainder will eventually return either here or to another asylum.

POST-MORTEM RECORDS IN 30 CASES (5 INCOMPLETE) FROM DR. CANDLER'S NOTES.

Obvious external signs of syphilis.—Scars suggestive of syphilis were present in 8 cases, and in three others there was a history of repeated miscarriages on the part of the wife.

Heart.

The left ventricle was hypertrophied in 9 cases.

„ „ „ „ „ wasted „ 5 „
 „ „ „ „ „ appeared to be natural „ 10 „

In all cases in which the heart was wasted the coronary arteries were exceedingly atheromatous, and in those cases with hypertrophied left ventricles the coronary arteries were either not diseased or, if attacked, there was but little stenosis of the lumen.

On the other hand, an enlarged left ventricle *may* be associated with gross disease of the coronary arteries. The coronary artery shown in Fig. 1 was taken from a heart the wall of whose left ventricle was immensely thickened. Here, however, the enlargement was mainly fibrous, the heart wall being very tough, while great strands of fibrous tissue running in its substance were easily conspicuous to the naked eye. The patient had died of generalised arterio-sclerosis of syphilitic origin.

Atheroma of the aorta was present in 27 cases, only slight in four of these.

There was atheroma of the aortic valves in 16 cases.

„ „ „ „ „ mitral „ „ 12 „
 „ „ „ „ „ coronary arteries in 23 cases.

The cerebral vessels were described as grossly atheromatous in four cases, of moderate grade atheroma in 10 cases, of slight grade atheroma in three cases, and natural in eight cases.

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The kidneys were described as being :—

Natural	In 7 cases.
Slightly fibrotic	„ 8 „
Moderately fibrotic	„ 3 „
Markedly fibrotic	„ 2 „
Granular	„ 3 „

There was pyelonephritis in one case and a pyæmic kidney in one case.

The renal arteries were markedly diseased in 12 cases.

Comparing these 25 post-mortem kidneys with the 36 clinical cases in which the urine was examined, the 21 cases out of 36 in which the urine was apparently normal, if contrasted with those in which the kidneys were described as natural, plus those described as slightly fibrotic (15 cases out of 25), the percentage, without labouring the point unduly, would be nearly the same in both instances, *i.e.*, 58·3 and 60 per cent. respectively.

Three brains showed macroscopic softenings, and in four brains there had been either recent or old hæmorrhages.

In nine cases there was either active or obsolescent tuberculosis of the lungs.

As is shown by the figures given in the preceding paragraphs some degree of arterial degeneration is almost universal in these cases, though the distribution varies considerably and by no means affects all the arteries equally.

Most commonly the aorta is attacked, and the type of degeneration is either that of the atheromatous plaque, with or without calcification, or of the patch of pearly-white fibrosis which is usually considered to be always caused by syphilis.

The valves may or may not be affected, but the aortic ring usually shows some degeneration either to a greater or lesser degree.

The peripheral arteries, including the cerebral, may occasionally be healthy or may present generalised thickening of their walls throughout the entire arterial system, or more usually such thickening may be confined to the arteries of certain regions of the body. Superadded to either of these conditions there may be plaques of nodular arterio-sclerosis in the formation of which the part taken by syphilis is probably very considerable. (Mott, "System of Syphilis.") *Vide* Fig. 3 showing a nodule produced by peri- and endo-arteritis.

Osler ("System of Medicine") gives the following three ætiological groups of arterio-sclerosis :—

1. *Involutionary*, caused by the ordinary wear and tear of life, and present to some extent in most people over the age of 40.

2. *Toxic group*, in which the degenerations are caused directly by the poisons of acute and chronic infections and intoxications.

3. *Hyperpietic group*, in which the degenerations follow long and persistent high arterial tension. In most persons between the ages of 50 and 60 years the first and third of these ætiological factors are probably present in varying degree, and in many persons, and apparently particularly in lunatics, the toxic group is superadded.

It is usually impossible to assign accurately their relative values to these three causes in any given case. However, plaques of pearly-white fibrosis are usually considered to be of syphilitic origin, and these were very frequent in the post-mortem cases under discussion.

Heubner was of the opinion that syphilitic arteritis always ends in fibrosis and never in atheroma, but Mott ("System of Syphilis") thinks that this statement is too sweeping in character and, in addition, thinks that the syphilitic virus may weaken the muscular fibres of the arterial system, thereby lessening the resistance to other causes that produce atheroma. Thus syphilis acts directly and indirectly in the causation of arterio-sclerosis.

A section of a patch of nodular arterio-sclerosis of syphilitic origin is shown in Fig. 3. There is peri-arteritis with small celled infiltration, marked increase of the intima (endo-arteritis), with hyaline degeneration and fibrosis, and there is degeneration of the elastic lamina of Henle, which is seen to be swollen. Fig. 6 shows the degeneration of the elastic elements, which are broken up and scanty, in an arterio-sclerotic artery.

Evidence of the varying and, one might almost say, capricious distribution of the arterial disease is afforded by the following instances:—

In 15 cases where the renal vessels were unaffected either the coronary arteries, the aorta or cerebral vessels were extensively involved.

G. M.—A general paralytic, presented atheroma only of the aorta and coronary arteries.

R. N.—A tabetic general paralytic, presented very extensive pearly fibrosis of the aorta and some degeneration of the coronary arteries, but the cerebral and renal arteries and the arteries of the extremities were unaffected.

W. S.—An elderly dement (not included in the present series), presented during life all the signs of a typical mitral stenosis. After death the transverse arch of the aorta was found to be covered with extensive areas of pearly-white fibrosis and the mitral ring was markedly stenosed, hard and fibrous. The aortic ring, however, and the ascending arch of the aorta had escaped altogether and appeared to be absolutely healthy. There was also a large area of syphilitic fibrosis involving much of the upper lobe of the left lung.

The mitral stenosis in this case was apparently of syphilitic origin, and it was remarkable that the aortic ring and ascending arch should have been totally unaffected.

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Changes in the brain.—Apart from cases of general paralysis there is usually a certain amount of generalised wasting of the convolutions with thickening of the pia and arachnoid mater, while the cerebral vessels are often obviously diseased.

Softenings easily recognisable to the naked eye were present in three brains. Thus T. G. had an extensive softening in the region of the right collateral fissure about $2\frac{1}{2}$ inches long and about 1 inch in width (*vide* Figs. 3 and 4, which show sections of his basilar artery). Other softenings may be no larger than a pin's head, as in the case of a woman (not included in this series) who died of generalised syphilitic arteritis and who presented the clinical picture of general paralysis. In her brain there were many such minute softenings together with many minute hæmorrhages, one of which is shown in Fig. 2.

Extensive hæmorrhages occurred in four instances, and hemiplegia from thrombosis or embolism is not infrequent in this class of case.

It must be remembered that with arterio-sclerosis the blood tension may be high or low. In the former case hæmorrhage is likely to occur, and in the latter thrombosis may supervene (Mott, "System of Syphilis," Vol. IV).

Microscopic investigation.—Excluding cases of general paralysis the following changes may be found :—

Meninges.—The arachnoid and pia mater are not often perfectly normal. Usually some thickening of these structures exists and is well marked in many instances. The small arteries may show peri- and endo-arteritis with narrowing of the lumen and hyaline degeneration of the wall. These chronic inflammatory processes in the meninges cause interference to the lymphatic channels, and the lymph spaces may become choked with debris and, if the condition is advanced, may materially damage the drainage system of the brain so that excess of fluid, probably charged with toxic products of degeneration, is apt to accumulate both in the sub-arachnoid space and in the ventricles of the cerebrum.

The walls of the fourth and lateral ventricles in old-standing cases frequently present granulations similar to those met with in cases of general paralysis.

At the periphery of the cortex the tangential fibres are lessened in number and exhibit fatty globules along their course, but are not so profoundly affected as in the brains of general paralytics.

Glia proliferation at the periphery of the cortex is almost invariable and may be a very prominent feature (*vide* Fig. 10).

In the ganglion cell layers the cells show degenerative changes; there is frequently shrinkage of individual cells within their peri-cellular spaces. Nissl granules and the intracellular fibrils are more or less broken up, and pigmentary and fatty granules are often present.

Fine pigmentary granules are found almost constantly in the ganglion cells of elderly subjects; they are unaffected by ether and, with the exception of osmic acid, do not take up fat stains. The larger fat globules stain readily with Scharlach R and may be present in considerable quantities both in the ganglion cells themselves and in the satellite cells which surround them.

Fat globules are found also in glia cells and in the walls of vessels of every calibre, from large arteries, as in the section of the popliteal artery shown in Fig. 5, down to the arterioles and capillaries of the brain substance itself (Plate II).

Bevan-Lewis ("Text Book of Mental Diseases") is of the opinion that "the glia cells become the phagocytes or scavengers of the tissues and thrive and multiply upon the degenerating masses of nerve cells."

Certainly where slow degeneration is going on the glia elements seem to thrive and increase marvellously well, and the frequent presence of fat globules in the substance of the glia cells would seem to lend support to this phagocyte theory.

Following Alzheimer, whose work on cell degeneration is so well known, the writer stained sections from several brains with hæmatoxylin and Scharlach R, and Plate II shows the distribution of the fat globules arranged around the glia nuclei near the walls of the small vessels and within the substance of the ganglion cells.

The writer also wished to demonstrate the presence of fat globules in the glia cells together with the processes of the cells in the same section and at the same time.

After many abortive attempts success was eventually attained by combining Marchi's osmic acid method with Ranke's stain for glia elements (Plate I).

Extensive glia proliferation is well shown in Fig. 10, taken from a case of senile dementia. Fig. 12 shows a large horse-tail glia cell, and the intimate connection of a glia cell to a small arteriole can be seen in Fig. 11.

Résumé of the Case of T. G.—From which Figs. 3, 4, 8 and 9 are taken.

Age at onset, 56. Age on admission to asylum, 59. Age at death, 59.

(From wife.)—For 33 years a carpenter in the Royal Navy. Was on the West Coast of Africa for four years. Married in 1879. Eight full-time children and one miscarriage, the last.

Family history.—Nothing known.

Drink.—No; lately has been an abstainer.

Temperament.—Very excitable, gloomy, sullen, obstinate, sleepy, and a very violent, uncontrollable temper. No previous insanity.

At onset.—"Has been very violent for the last 2½ years. I had to leave him 11 months ago. He threatened to do for me, showing me naked razors and carving knives. I went in fear of my life."

Suicidal.—Has frequently threatened to cut his throat or to shoot himself.

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On admission (from clinical notes).—He is the subject of dementia; his memory is very defective. Has no idea of time and space, does not remember the month or year or when he came here. Restless and wandering at night. Unable to give any account of his previous life.

Circulatory system.—Pulse 68. Hypertrophied left ventricle. Systolic bruit at apex. Second aortic sound plus. Arteries atheromatous.

Urine.—1.035, acid. No albumen.

Nervous system.—Tremors of hands and face.

Pupils.—Dilated and equal. Consensual reflex, sluggish; iridoplegic reflex, sluggish to light. Knee jerks very sluggish. Superficial reflexes not obtained. Arcus senilis is present.

Sphincters.—Incontinence of urine and fæces.

The patient subsequently developed gangrene of the feet and broncho-pneumonia and died.

Post-mortem notes.—Scar in left groin probably syphilitic.

Head.—Some excess of fluid in the subdural space. Thickening and opacity of the pia-arachnoid. Some excess of fluid in the sub-arachnoid space. Cerebral vessels atheromatous (Fig. 3).

Brain.—Of average pattern, congestion of superficial vessels and thickening of the pia-arachnoid. Generalised wasting of the convolutions. Old cortical softenings on the under surface of the right temporal lobe and along the left Sylvian fissure.

Lungs.—Emphysematous, some patchy broncho-pneumonia. No tubercle.

Heart.—Large. Left ventricle hypertrophied. Left auricular appendix contained a thrombus adherent to its walls. Some stenosis and thickening of the mitral curtains and chordæ tendinæ. The aortic valves are atheromatous and in places calcareous. The coronaries show moderate grade atheroma without diminution of their lumens or calcification.

Liver.—Fatty, with some chronic congestion.

Kidneys.—Very markedly sclerotic, with depressed areas in places suggestive of old infarction. A small oxalate calculus in left kidney.

Renal arteries.—Thickened.

Abdominal aorta.—Atheroma of moderate grade, no calcification.

Cause of death.—Gangrene of both feet with septocæmia, broncho-pneumonia, renal fibrosis and generalised arterio-sclerosis.

Other conditions present.—Pulmonary emphysema, cholelithiasis, renal calculus, mitral stenosis, old softenings of *cortex cerebri* thrombosis of the left popliteal vein.

Microscopic investigation.—Partial degeneration of the ganglion cells, glia proliferation, fat globules in the glia cells and in the walls of the small blood vessels.

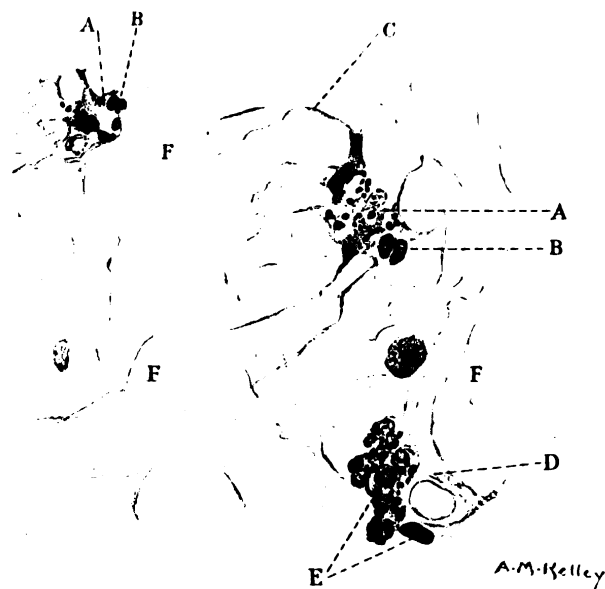


PLATE I.

Section of the cortex of W. M., a senile dement with gross arteriosclerosis of the cerebral vessels. Stained by a combination of Marchi and Ranke's methods to demonstrate glia cells with their processes and fat granules, at the same time and in the same section.

A.—Glia cells.

B.—Fat granules contained therein.

C.—Processes of the glia cells.

D.—A ganglion cell.

E.—Satellite cells surrounding the ganglion cell containing fat granules.

F.—Fine network of glia processes.

Magnification 500.

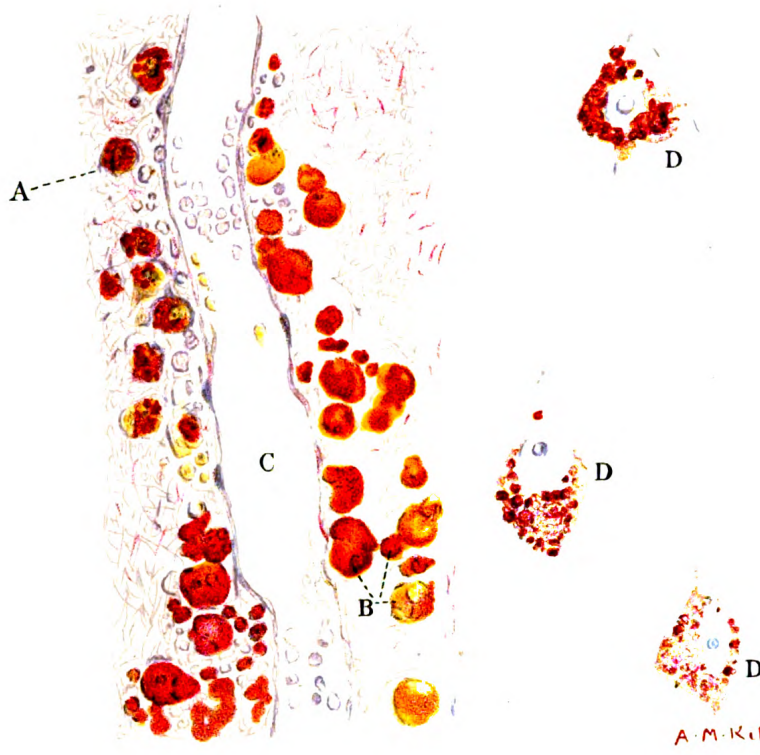


PLATE II.

Section of the cortex of W. M. (as in Plate I), stained by Scharlach R, showing the distribution of degenerative fat granules.

- A.—Fat granules surrounding the nuclei of the glia cells.
- B.—Fat granules lying just outside the vessels.
- C.—A capillary.
- D.—Ganglion cells containing fat granules.

Counterstained with hæmatoxylin.

Magnification 500.

Heart Muscle.

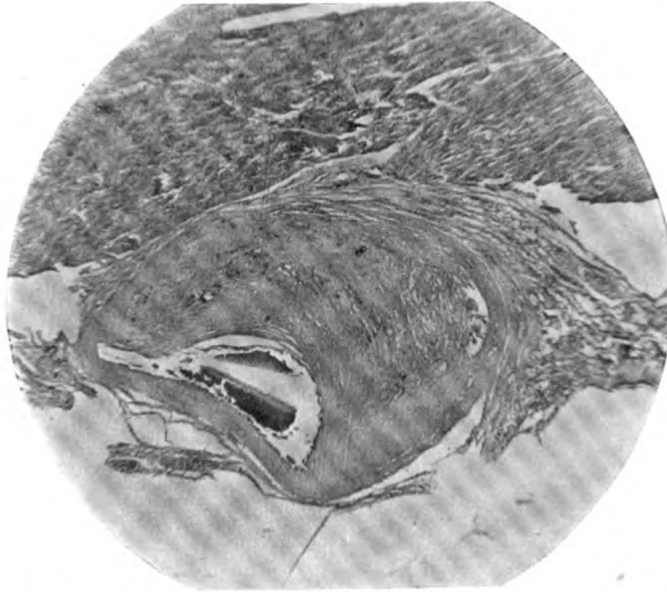


FIG. 1.—*Syphilitic coronary artery* from a woman of 44 years who died with generalised arterio-sclerosis. Clinically she was considered a general paralytic. The section shows marked obliterative endo-arteritis with hyaline degeneration. The heart itself was large with greatly thickened walls of the left ventricle, which were tough and fibrous even to the naked eye. Magnification 35.

Thickened
Meninges.

Vein.

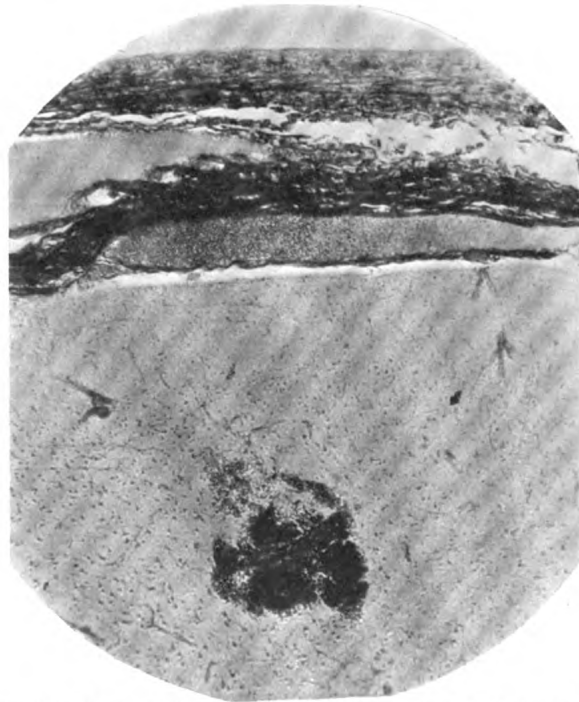
Minute
Hæmorrhage.

FIG. 2.—Section of the brain cortex from the same case as in Fig. 1, showing a miliary hæmorrhage, of which there were great numbers throughout both the brain and spinal cord. Death was caused by an extensive hæmorrhage in the region of the basal ganglia. The meninges are seen to be much thickened. Magnification 35.

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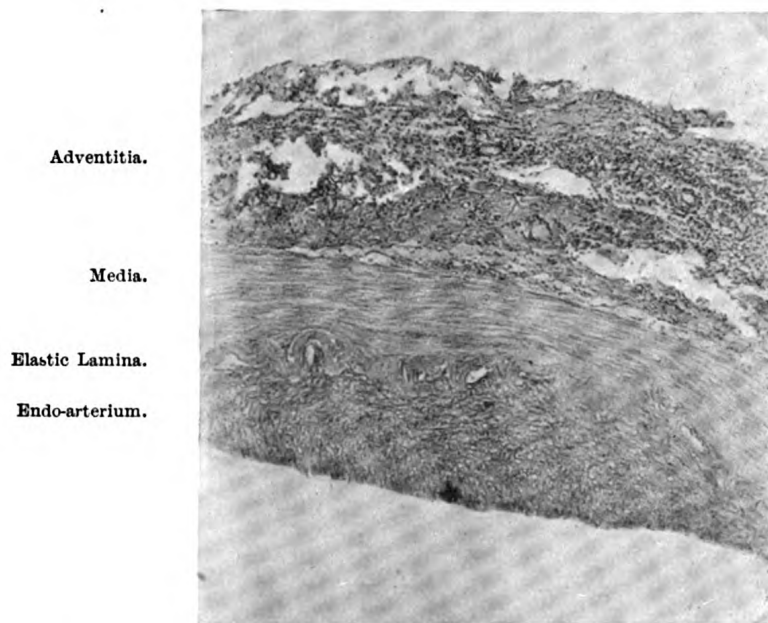


FIG. 3.—Section of a nodular arterio-sclerotic plaque from the basilar artery of T. G., whose insanity commenced when he was aged 56. There is thickening of the adventitia with small celled infiltration (peri-arteritis). There is some change in the elastic lamina of Henle, which appears swollen. Endo-arteritis is also present. Magnification 80.

A fuller description of the case from which these figures are taken will be found in the text, pages 205–206

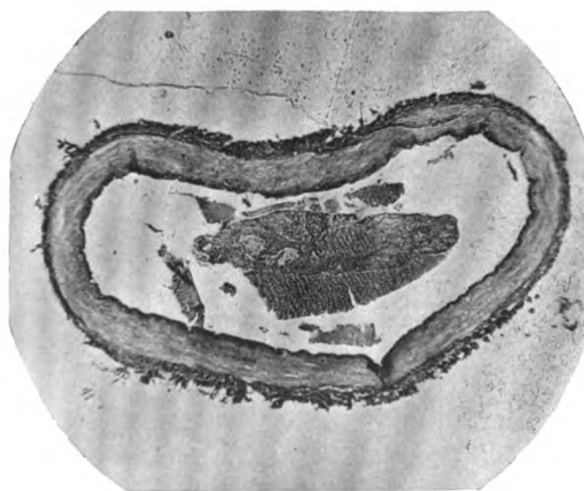


FIG. 4 (to compare with Fig. 3).—Another section of the same basilar artery (low power). There is but little change either in the adventitia or endarterium. An instance of the localised nature of the lesions in the nodular form of arterio-sclerosis.

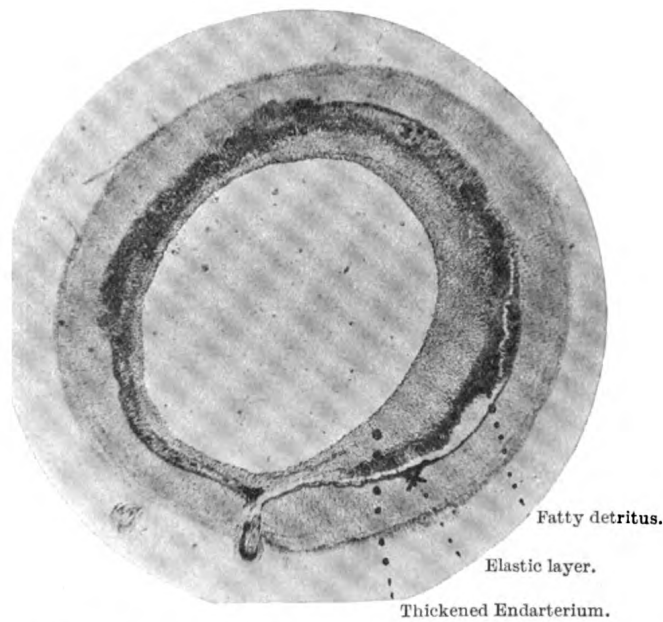


FIG. 5.—Section of the popliteal artery of an elderly dement, stained with Scharlach R. The fatty detritus which has taken up the stain is seen to be entirely internal to the elastic layer of Henle.

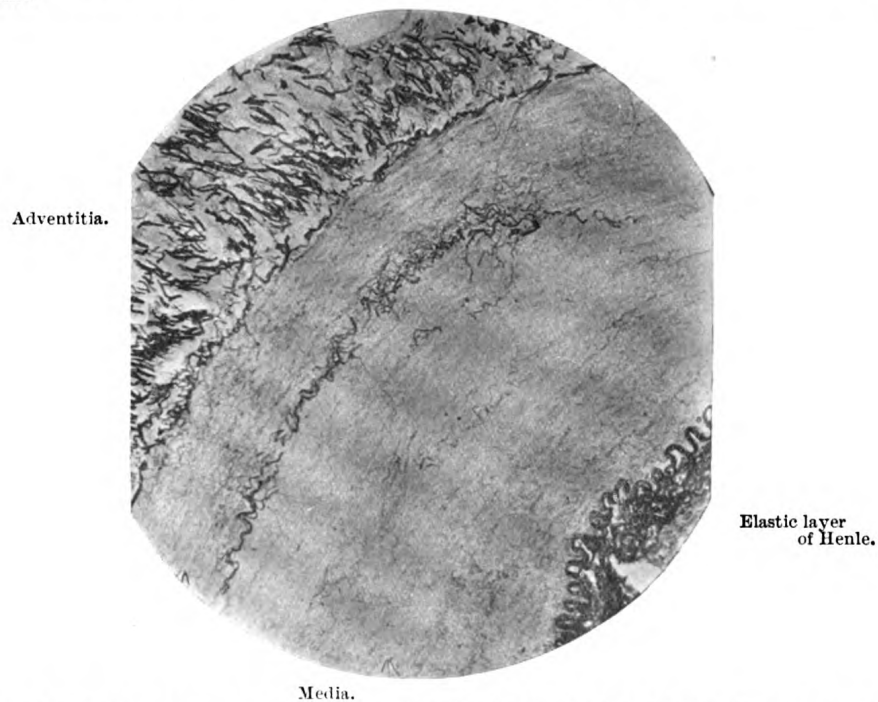


FIG. 6.—Section of an arterio-sclerotic artery (post. tibial), stained with Fuchsin resorcin to show the elastic fibres. These, in the media, are seen to be diminished in number and to be broken up. Magnification 200.

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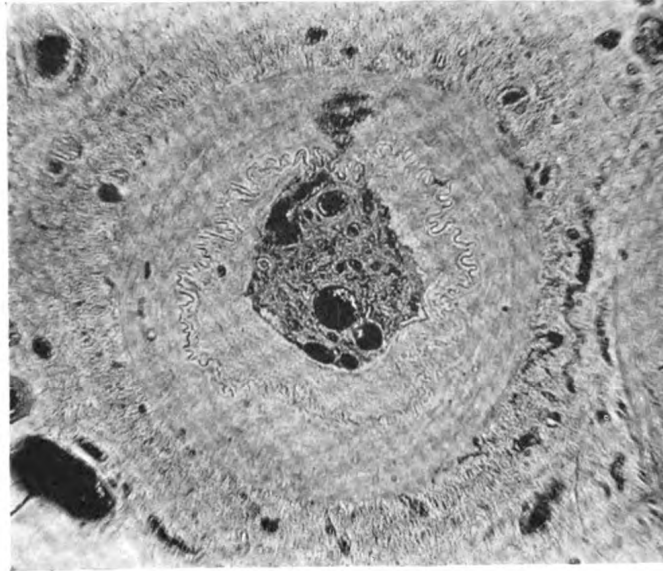
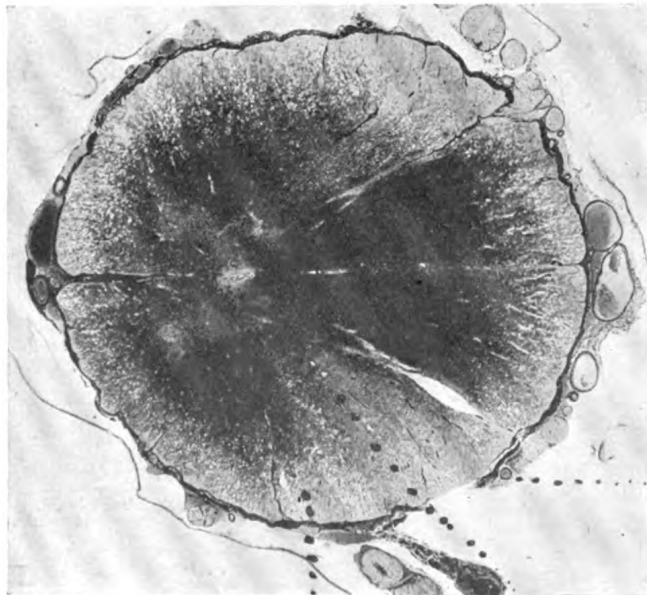


FIG. 8.—Section of the left posterior tibial artery of T. G., whose insanity commenced at age of 56. See also Figs. 3 and 4. Patient died with extensive gangrene of both feet. The section shows marked endarteritis with an organised thrombus practically obliterating the lumen of the vessel.



Thickened Artery.

FIG. 7.—Section of the dorsal region of the spinal cord taken from the same case as Figs. 1 and 2. The meninges are thickened and there is an annular sclerosis at the periphery completely surrounding the cord. The crossed pyramidal tracts are degenerated. The case was one of generalised syphilitic arterio-sclerosis. The magnification is unfortunately not high enough to show the thickened arteries very well, nor to demonstrate the minute hæmorrhages which were numerous throughout the cord. (Weigert Pal and eosin.)

Annular
Sclerosis.

Degenerated
Crossed
Pyramidal
Tract.



Endophlebitis.

Media.

FIG. 9.—Section of part of the wall of the left popliteal vein from the same case, T. G. This vein exhibits endo-phlebitis corresponding to the endarteritis found in sclerotic arteries. Magnification 80.



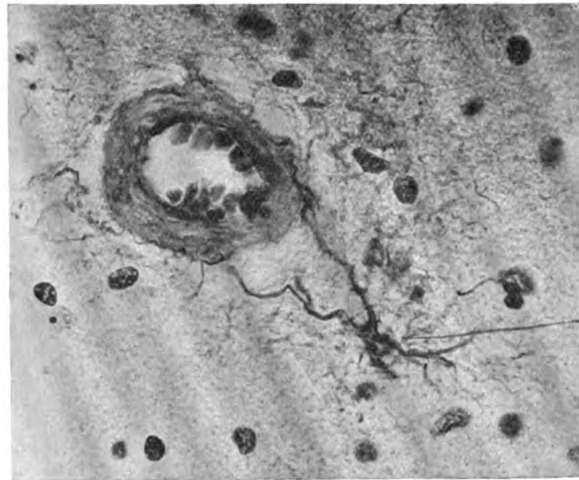
Horse-tail cell.

Small Sulcus.

Small Capillary
surrounded by
glia cells.

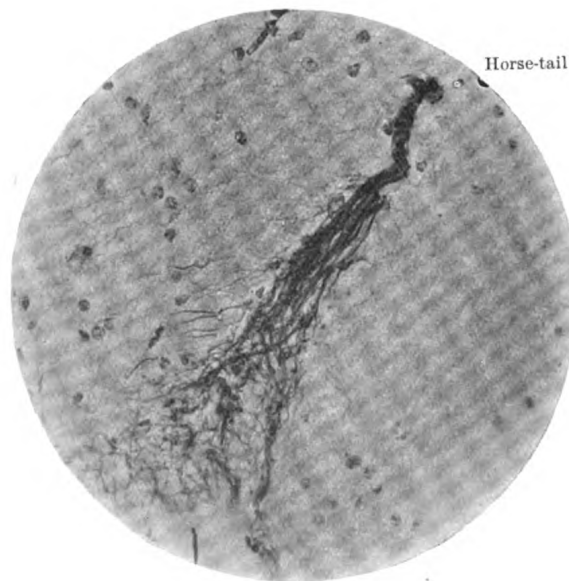
FIG. 10.—Section of the cortex of the brain of W. M., a senile dement with gross sclerosis of the cerebral arteries, stained by Ranke's method. This section shows a mass of neuroglial elements at the edge of a small sulcus. There is a tangled mass of glia processes with star-shaped and horse-tail glia cells. Magnification 250.

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Glia cell.

FIG. 11.—From cerebral cortex of the case from which Figs. 1 and 2 are taken. Glia cells attached by its processes to an arteriole. Ranke's stain. Magnification 300.



Horse-tail processes.

Small sulcus.

FIG. 12.—From cerebral cortex of W. M. Horse-tail glia cell. Ranke's stain. Magnification 300.

The family and personal history would appear to be of importance in cases of insanity occurring in the involutional period, as in most other types of insanity.

Family history.—The difficulty experienced in obtaining family histories is considerable. It is found that there is much reluctance on the part of the relatives to give information on this point. Frequently the replies given to questions are evasive and may be proved subsequently to be untruthful. In this series of 104 cases there were 51 cases in which some family taint was found. In the remaining 53 cases it is impossible to say from the information obtainable how many were free from family taint or not. Many of the papers were returned blank, and the majority with "not known" scrawled across that part of the form. Some of the patients seem to have no friends or relatives, and in these cases of course little information is available.

Of the 51 cases with a positive history, three were of phthisis only; viz., (1) one brother; (2) father and mother; (3) mother. Four were of alcohol only, viz., (1) four brothers, drunkards; (2) mother, drunkard; (3) father, drunkard; (4) aunt, drunkard.

In two cases the only available information consisted in the vague statements that "the father died in a fit" and that "an uncle died of paralysis" respectively.

In the remaining 40 cases there was a definite history of insanity in one or more near relatives. They may be tabulated as follows:—

	Grandparents.	Great Grand-parents.	Father.	Mother.	Children.	Brothers and Sisters.	Uncles.	Aunts.	Cousins.	Nephews and Nieces.	Total.
Insane	2	...	7	1	4	17	3	4	2	3	43
Drunkards	2	1	6	4	1	6	...	1	21
Epileptics	1	...	1	...	1	3
Suicides	1	...	1	...	1	1	...	4
Imbecile	1	...	1	2
"Nervous"	1	1	2
"Died in a fit"	2	1	1	4
"Died of paralysis"	2	1*	3
Total	6	1	17	10	8	24	5	5	3	3	82

* Alive, paralysed.

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In addition to these figures there were 19 cases of phthisis in 10 families. In all probability this figure is very much smaller than the correct one.

Some of the family histories are worth looking at more closely, and I have appended a few of the more striking.

A. C.—Onset of insanity, 50. Mother had 10 children and six miscarriages. Of the 10 children, the patient is in Claybury, three sisters are in asylums and one brother committed suicide. There is no information as to the remaining five children. The patient himself had four children who are said to be healthy.

J. V. H.—Onset of insanity, 50. Drank to excess for years. Definite history of syphilis. His father, grandfather, great-grandfather, and a paternal cousin were drunkards and “a little alcohol made them mad.” The grandfather and the cousin attempted and committed suicide respectively. His maternal grandfather died of phthisis. Patient was unmarried.

J. L. S.—Onset of insanity, 53. Alcoholic mania. Grandfather, drunkard ; father, drunkard ; and paternal uncle, insane ; patient, insane ; son, epileptic. In this case, as in the preceding, we have four generations involved.

T. C.—Onset of insanity, 57. Had delirium tremens twice before admission to asylum. Father’s side had a “bad history.” Father died in a fit. Four of patient’s brothers were drunkards.

I. C.—Onset of insanity, 53. No history of drink. Both father and mother phthisical.

G. P.—Onset of insanity, 50. Father, epileptic ; mother, drunkard.

R. E.—Onset of insanity, 50. Temperate. Mother died of paralysis. A brother died in Colney Hatch. A sister is an imbecile. Two brothers and two sisters died of phthisis.

W. T. D.—Onset at 57. Father, insane ; patient, insane ; one son drunkard and attempted suicide ; three sons died of phthisis.

W. H.—Onset at 55. Patient, insane ; sister, insane ; three brothers and one sister died of phthisis.

A. S.—Onset of insanity at 52. Huntingdon’s chorea :—

Father died of Huntingdon’s chorea	aged	47
Patient	„	54
Patient’s sister	„	(?)

Another sister has the disease and is in an asylum. Patient has a son aged 20, at present healthy.

G. H. M.—Onset of insanity at 60 years. Senile mania. Father, drunkard, died in an asylum ; aunt, insane ; patient, a heavy drinker, died in asylum ; daughter is in an asylum.

Occupation.—As regards occupation, nearly every calling open to the lower and lower middle classes seems to be represented :—

Sailors	13
Waterside workers (lightermen, dock labourers, &c.)	7
Army	7
Skilled artizans	15
Carmen, barmen and commercial travellers	12
Unskilled labourers	7
Painters	6
Small shopkeepers	5
Hawkers	5
Clerks	4
Porters	3
Salvationists	2
Various	18
Total	104

It will be seen that the services and waterside labourers account for 27 cases. Taking into consideration, however, the free and easy manners of soldiers in the tropics and of sailors when ashore, such preponderance is not altogether surprising. Carmen, barmen and commercial travellers have been bracketted together for the reason that in hardly any other professions are the facilities for drinking to excess so continually present.

The comparatively large representation of painters is interesting inasmuch as five out of the six cases suffered from very marked arterio-sclerosis. It is not impossible therefore that in these cases lead may have been a factor in the production of the mental breakdown.

Alcoholism.—According to the notes there had been a definite history of alcoholism at some period in the patient's life in 51 cases, that is in nearly 50 per cent.

In numerous instances such over-indulgence is of many years duration, but in others it would appear to have been of recent or fairly recent development. Thus, in certain cases the patient does not seem to have drunk heavily until the mind and will power had already begun to fail from other causes, and in these cases it is pardonable to consider the alcoholism as a symptom of the mental disease; though it must be recognised that such indulgence, though primarily a symptom, will itself react most unfavourably on the patient's mental state, thus establishing a vicious circle.

Similarly, other patients had not started drinking until after the occurrence
(16147)

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of some mental or physical shock or until domestic worry and privation had driven them to seek oblivion in the public-house.

Other evidence that neuropathic taints have tended to weaken resistance to alcohol is afforded by the statement volunteered in two cases by friends "that a very little alcohol would upset the patient." Furthermore, mental instability is indicated in 12 cases in which the patient was intemperate only in bouts with alternating intervals of complete or comparative sobriety.

Such may often be regarded as instances of recurrent insanity where the mental disorder by diminishing the patient's self-control has tended to induce excess of all kinds.

Injuries.—The exact relationship of an injury to mental disease, as medico-legal reports show, is often enough a difficult matter. This is so even when the patient is under observation immediately after the accident and for some months subsequently. It is still more difficult when a case is investigated in an asylum some time after the accident, when reliable evidence is unobtainable or scanty.

An injury may be the primary cause of mental disease, though only rarely, as is shown by Dr. Mott in a paper read before the British Medical Association in August, 1911. An interesting case is described by Dr. Robert Jones in Vol. III of the "Archives of Neurology."

A young man, aged 26, of excellent character, a total abstainer and with no family taint, met with a serious head injury. Subsequently he developed marked moral obliquity with dementia and was transferred to Claybury Asylum from one of His Majesty's prisons.

An injury may be a contributory factor in the causation of insanity or a mere coincidence only, or conversely a pre-existing mental disorder by inducing a fit or seizure at an inconvenient moment may directly precipitate a serious accident. For example :—

W. D.—Age at onset, 57. Father was insane. The patient, who had been a sailor for 32 years was treated for right hemiplegia (? specific) at Greenwich Hospital 10 years ago and recovered. Wassermann reaction on the blood is positive. He went for a walk with his eldest son (who gave him a black eye), both being the worse for liquor. From that time his memory failed and he became confused, *i.e.*, he would put his clothes on the wrong way and forget what he was going to do next. Subsequently he attempted to strangle his son. After the lapse of a year he is still demented and amnesic. (History given by a younger son.)

S. P.—Age at onset, 55. His father and mother both drank, and the former died in an asylum. The patient was said to be temperate. He sustained a fall with concussion a few days before onset. He behaved oddly

in the street, was sentenced for being drunk and disorderly, and was transferred to Claybury from Pentonville Prison. He was discharged recovered after two months' detention.

G. S.—Age at onset, 59. He has a sister in an asylum. He sustained a severe fall 10 years ago for which he was operated upon at University College Hospital for "tetanus." He had another fall 12 months before onset, after which he became melancholic, drank hard, and tried to cut his throat with a razor. He was eventually discharged recovered.

H. B.—Age at onset, 54. Formerly in the Royal Navy. No family history known. Temperament excitable, and he would drink in bouts. He fell on a curb and sustained a fractured skull (verified by the police report). On admission to the asylum he was confused and disorientated. He was eventually discharged recovered.

R. H.—Age at onset, 54. Grandmother died in an asylum. No history of drink. Had a "severe fall on head" two years before onset. At present he is melancholic with delusions of persecution.

G. F. P.—Builder and decorator. Formerly in Army for seven years. Has drunk heavily all his life. He has a stricture of the urethra and there is a definite history of syphilis. The Wassermann reaction is doubtful, hæmolysis occurring but very slowly. He is suffering from dementia (? alcoholic) with delusions of persecution. Shortly before the onset of his mental symptoms he fell through a skylight. The exact details are not known, but the shock to a man with such a personal history must have been considerable, and the mental breakdown may or may not have been precipitated by "commotio cerebri" of traumatic origin.

Syphilis.—Between the ages of 35 and 45 the subjects of general paralysis account for most of the cases in which syphilis is a prominent ætiological factor of insanity. But in the succeeding one and a half decades general paralysis is less common, and in its stead the slow sclerosing changes of arterial syphilis begin to make their insidious onset felt.

Dr. Mott ("System of Syphilis," Vol. IV) says: "Syphilis is probably the most important factor in the production of arterio-sclerosis, especially cerebral arterio-sclerosis," and judging from the almost universal presence of arterio-sclerosis in the present series of cases it would appear that this disease would rank with hereditary nervous instability in the ætiology of involutional insanity. At the same time it is difficult to dogmatise on this subject, for a positive history of infection is not always easily obtainable. External stigmata of the disease are not invariably present, and when they are present are not always reliable. By the time the patient has become insane the disease may be 20 or 30 years antecedent and all traces of active trouble

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may have vanished, and only a greater or less degree of arterial degeneration is left to indicate the probability of an attack of syphilis. Out of 104 cases of insanity occurring between the ages of 50 and 60, only in 11 was a history of infection established beyond all doubt, and in 11 more the infection was practically certain.

From the writer's experience the Wassermann reaction would appear to have only limited utility in this class of case. Dr. Candler and Mr. Mann were kind enough to apply this test (in its original form) at the Claybury Laboratory to the serum taken from 19 cases. Excluding three cases of general paralysis, a positive reaction was obtained in three cases, whereas with some of those that were negative there was a clear and definite history of syphilis, and in some others there was strong presumptive evidence, though no actual proof. It might be reasonably expected that after the lapse of a great number of years the infection may have worn itself out.

There is not sufficient evidence in this series of cases to show the extent to which diseases other than syphilis have contributed to the mental breakdown. In perusing the notes of these patients one finds mention here and there of previous attacks of such diseases as small-pox, malaria, yellow fever, influenza, typhoid, &c., and doubtless such attacks may in some cases have influenced the patient's mental powers either at the time by the action of toxins on the nervous system or more indirectly by favouring the onset of arterial degeneration.

In the notes of 30 post-mortems active tuberculosis of the lungs was present in five cases and obsolescent tubercle in six cases. Osler, in the chapter on arterio-sclerosis in the "System of Medicine" (Osler and Macrae) states that arterial degeneration is very frequent during attacks of scarlet fever, measles, diphtheria, small-pox, typhoid fever, and other acute infections.

Conclusions.—1. A family history of neuropathic taint is extremely common. Out of 104 cases, 51 had some family history either of insanity, epilepsy, alcohol or suicide, and in the majority of the remaining cases (53) no reliable information either negative or positive on this point could be obtained.

2. There had been excess of alcohol at some period in the patient's life in 50 per cent. of the cases.

3. An injury may be considered a contributory factor in the causation of an attack of insanity.

4. *Syphilis.*—In 21 per cent. of the cases an antecedent attack of syphilis was either definitely known to have occurred or was practically certain. Judging from the almost invariable presence of arterio-sclerosis and from the frequency with which syphilitic patches of nodular arterio-sclerosis were found post-mortem, the percentage of patients who had at some time or other contracted the disease is probably much higher than that given.

5. The preponderating mental state of these patients is melancholia, usually complicated with delusional insanity and a varying degree of dementia. Thirty-one patients have shown suicidal and 19 homicidal tendencies.

6. In less than a third of the cases the patient had recovered sufficiently to be discharged from the asylum, but relapses are not uncommon.

7. Arterio-sclerosis is extremely common, but gross kidney disease is uncommon and albumen in the urine is not often present.

8. Some or other of the following morbid changes may frequently be found in the brain and cord :—

Thickening of the cerebral and spinal arteries.

Thickening of the meninges.

Excess of fluid in the serous spaces in and around the brain and cord.

General wasting of the convolutions.

Granular ventricles.

Naked eye and microscopic hæmorrhages in the brain substance and meninges. Naked eye and microscopic softenings in the brain.

Degeneration of the ganglion cells and tracts of the brain.

Proliferation of the glia elements.

Presence of fatty degeneration products in the ganglion cells, glia cells, and in and around the arterioles and capillaries of the brain.

The writer would like to take this opportunity of expressing his gratitude to the following :—

To Dr. F. W. Mott (Director of the Pathological Laboratory of the London County Asylums) for suggesting the investigation, and for his help and kindly interest.

To Dr. Robert Jones (Medical Superintendent of Claybury Asylum) for the encouragement he has given, and for permission to make use of the asylum case books.

To Dr. J. P. Candler (Assistant Pathologist to the London County Asylums) for his ungrudging assistance and many courtesies.

To Dr. J. P. Candler and Mr. Sydney Mann for applying the Wassermann test to the serum of 19 cases.

To Mr. Chas. Geary for his advice on histological methods and for producing the photomicrographs.

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Cortical Cell-Lamination of the Hemispheres of some Rodents.

By DR. A. B. DROOGLEEVER FORTUYN.

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INTRODUCTION.

The following researches were begun in the Pathological Laboratory of the London County Asylums, where the Pathological Sub-Committee of the London County Council kindly permitted me to work. They were continued in the Zoological Laboratory of Prof. Dr. C. Ph. Sluiter, University of Amsterdam, and finished in the Central Dutch Institute for Brain Research at Amsterdam.

I wish to express my great thanks to Dr. F. W. Mott, F.R.S., Director of the Pathological Laboratory, Claybury Asylum, for many valuable suggestions and for his kind assistance in many respects. I desire to thank Prof. Sluiter for his helpful interest in my work and his kind permission to use the greater part of these investigations as a thesis for the degree of D.Sc. (Droogleeve Fortuyn, 1911). And finally I wish to acknowledge gratefully the influence which Dr. Ariëns Kappers, Director of the Central Dutch Institute for brain research, has exercised upon my work.

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In the third volume of the "Archives of Neurology," a paper by Mott was published (Mott, 1907) which was an effort to correlate the evolution of structure and function of the visual cortex in mammals.

And the results were successful. For from the Insectivora with poorly developed sight to animals like monkeys in which sight is the principal sense a series of animals was found in which as the function of the visual area became more complicated so the structure of it became more complex.

Two years later in the same periodical Ariëns Kappers wrote an article (Kappers, 1909) upon the comparative anatomy of the palaeocortex and archicortex of vertebrates. Kappers in some respects came to the same conclusions concerning the palaeo- and archicortex as Mott regarding the visual neocortex. Kappers' researches thus indicated a progressive evolution of the olfactory cortex.

At the suggestion of Dr. Kappers I undertook a similar investigation of the auditory cortex, and this I had the opportunity of commencing in the laboratory of Dr. Mott at Claybury.

Consequently I had to obtain the brains of mammals, differing widely in their auditory functions, and to study the anatomy of their auditory cortex. Generally speaking, we know better whether an animal has good sight and sees well than whether an animal is quick of hearing and depends much upon this sense in its adapting to environment. Direct observations concerning the development of hearing are relatively scarce, and I consulted the work of Gray (1908), where the internal ear of a great number of animals has been described and figured. I found this monograph a valuable guide in looking for animals with varying degrees of development of the auditory receptor apparatus.

I started with the expectation that the number of windings of the cochlea correlated with the number of cells of Corti, would be connected perhaps on the one hand with the development of hearing, and on the other hand with the development of the auditory cortex.

The number of cochlear windings differs greatly in different mammals, but most of all in animals belonging to the order of rodents. Gray found two to be the lowest number (in *Mus musculus*) and $4\frac{1}{2}$ to be the highest one (in *Hydrochoerus capybara*). According to Weber (1904), *Coelogenys* exceeds this number, for it has five cochlear windings. I concluded therefore that it would be better to limit my researches to the rodents.

This limitation offered, moreover, the following advantages. First, rodents in general are very easily obtained; secondly, the brains are of a relatively small size, and are lissencephalous; consequently, a thorough and systematic investigation of the cortical areas is less laborious and for comparison more reliable.

Furthermore, some animals like the rabbit, the guinea-pig, the rat and the mouse belong to the rodents, and their habits are better known than many other animals because they are used for medical and physiological researches. Again, we possess in the waltzing-mouse a rodent naturally deaf, whose auditory cortex should therefore offer an interesting field for comparative observation.

And finally, restriction to one order of animals offered the great advantage of a surer and simpler homologisation of the cortical areas in the different animals.

Notwithstanding all that has been done by Brodmann, Hermanides and Köppen, Mott, Schuster, Watson, and others, concerning the homologisation of cortical areas in animals belonging to different orders, it seems to me that much more work is required before sufficiently certain results are obtained.

That the danger of a wrong homologisation of cortical areas in animals of different orders is not imaginary is shown by the fact that Mott (1907), as well as Hermanides and Köppen (1903), in rodents look upon an area as the visual cortex, which is granular cortex (Körnerrinde) according to Brodmann (1906), and not at all homologous with the area striata, the visual cortex of other mammals.*†

Previously I thought to find in the work of Brodmann (1909) an easy guide to recognise in my preparations of the brain of rodents the auditory cortex (areas 20, 21 and 22 of Brodmann). In Brodmann's book the order of rodents is dealt with and complete maps of the brain of the rabbit and of spermophilus agreeing fairly well with one another, are given.

But I was deceived in this respect. The guinea-pig, accidentally the first rodent I studied, did not show areas which could be recognised as the areas 20 to 22 of Brodmann. Many other areas too could not be found, although they were carefully sought for or they were situated on quite another spot than would follow from the maps of Brodmann. This was also the case with the rat, the mouse and the squirrel, and lastly I could not even agree with Brodmann in many respects as to the rabbit, the animal which Brodmann has especially studied. I observed, however, that all rodents agreed with one another in the main principles.

Under these circumstances I was unable to recognise with any degree of certainty the limits of the auditory cortex of the rodents without homologising at the same time some of the neighbouring areas.

* Needless to say that the general results of Mott are not at all contradicted by this single fact.

† Mott has informed me that Brodmann's criticism is a just one; the specimens supplied to him by Watson of the shrew, the mole, the hedgehog, the rabbit, the chinchilla, the wallaby, the suricate, the camel and the mule deer were not his own. Although most of these are from the true visual area those of the camel and mule deer are certainly not.

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By doing this I became more and more convinced that the situations were more exactly seen by me than by Brodmann for this reason, that I found an accordance in all the rodents' brains which I studied.

So I decided to pursue still another purpose than the comparative anatomy of the auditory cortex, and to compose a series of brain-maps of rodents, based exclusively on data procured from the rodents themselves and comparing, these animals only *inter se*. I started my investigations upon quite another principle to Brodmann; he compared animals of various orders (including man) and homologised in this way several areas as demonstrated in the maps published by him.

I doubt whether these homologies of Brodmann are all true because according to my observation of the order of rodents I obtained results differing considerably from those of Brodmann, who tried to connect and relate this order to other orders.

I cannot yet explain in detail in what respects I agree with or differ from Brodmann. I will do this after the description of my results and their mutual comparison in the comparative chapter, page 332.

I will give there too a review of the work of other authors.

Two publications on the rabbit support the opinions of Brodmann. The first one is a paper of Zunino (1909), a pupil of Brodmann, who found when studying the fibro-architecture the same areas as Brodmann when studying the cell-lamination of the cortex. Of course, I cannot contradict Zunino's results in the absence of observations of my own. But they did not help me to recognise in my preparations where the cells were stained, the areas which may be seen there according to Brodmann.

The other publication is the atlas of frontal sections of the rabbits' brain, published by Winkler and Potter (1911) at a time when my investigations of the rabbit were nearly finished. As to the cortical areas Winkler and Potter follow Brodmann on the whole, but besides indicating the situation of the areas they describe their structure. This was omitted by Brodmann, and certainly did not simplify the recognition of his areas.

I will discuss this atlas afterwards, and will only remark that the intention to follow Brodmann as closely as possible had led, in my opinion, to some inaccuracies.

Because my results obtained with rodents deviate in general so far from those of Brodmann, and because I do not wish to homologise the areas found by me in rodents with those of other animals, I could not follow Brodmann's nomenclature of cortical areas. I gave a nomenclature of my own, only valid for the rodents, and indicated the cortical areas only with a letter and not with a name. I consider this nomenclature to be a preliminary one,

useful to explain clearly my results, but I shall be pleased to see, where sufficient reasons exist, my nomenclature replaced by that of Brodmann. By the work of Isenschmid (1911) and of I. de Vries (1911) on the mouse, it appears that other authors too are not willing to follow Brodmann in his nomenclature.

In choosing my material I laid stress upon representing as many families of rodents as possible. As might be expected, the maps of more nearly related animals resembled more one another than those of animals belonging to different families.

Out of the sub-order of Duplicidentata I examined, as representatives of the family of Leporidae, the rabbit (*Lepus cuniculus*) and the hare (*Lepus europaeus*).

Out of the sub-order of Simplicidentata I examined representatives of four families.

Out of the Sciuroidea I examined the squirrel (*Sciurus vulgaris*), out of the Myoidea the rat (*Mus decumanus*), the mouse (*Mus musculus*), and the waltzing-mouse (*Mus Wagneri* var. *rotans*),* out of the Hystricoidea coendu *prehensilis* and the guinea-pig (*Cavia cobaya*), the latter belonging to the sub-family of Caviidae, out of the Geomyoidea (*Dipodomys merriami nitratoides*). I chose *Dipodomys* on account of the well-known anomaly of its internal ear. In this animal the bullae tympani are so extremely enlarged, that they meet each other mesially above the skull.

Although my original purpose, the study of the relation of structure and function in the auditory cortex has been somewhat neglected by the extensive but necessarily preceding task of composing maps of the animals to be studied, I have not wholly lost sight of it.

In the chapter on the relation of structure and function of area *p* (the auditory cortex ?), I will describe my efforts to obtain my end.

That the result is entirely negative must be partly ascribed to the great difficulties which check us in such a research. To reveal these difficulties to other investigators has been my intention in writing this chapter.

In this chapter special attention has been given to the waltzing-mouse on account of its deafness.

MATERIAL AND METHODS.

The material used in these researches consisted of :—

- 3 specimens of *Sciurus vulgaris* (L.).
- 2 „ „ *Coendu prehensilis* (Lacep.).
- 2 „ „ *Lepus cuniculus* (L.).

* Refer for this name on Droogleever Fortuyn (1912).

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- 1 specimen of *Lepus europaeus* (Pall.).
- 2 specimens „ *Cavia cobaya* (Mareyr.).
- 2 „ „ *Mus decumanus* (Pall.).
- 3 „ „ *Mus musculus* (L.).
- 7 „ „ the Japanese waltzing-mouse (*Mus Wagneri* var. *rotans*).
- 2 „ „ *Dipodomys merriami nitratoideus*.

For one part of this material (*Cavia*, *Mus decumanus*, *Mus musculus*) I am indebted to Dr. F. W. Mott; for another part (*Sciurus*, *Coendu*, *Cavia*) to the Royal Zoological Society, "Natura Artis Magistra," at Amsterdam. I obtained *Dipodomys* by the kind accommodation of Dr. Grinnell, Director of the Museum of Vertebrate Zoology, University of California. Prof. Sluiter provided me with the tame rabbits, and my friend Dr. Swellengrebel with the hare. I wish to express here once more my thanks to these gentlemen.

Above all I am grateful for the waltzing-mice, which I got either by the kind assistance of Dr. Ariëns Kappers from Prof. Zwaardemaker and Dr. Quix at Utrecht, or from "Natura artis magistra." Dr. Kerbert, Director of this Society, imported, also for my sake, waltzing-mice from Vienna.

The way in which this material was fixed and stained was one of the many varying ways in which so-called Nissl-preparations may be made. I described this method fully in my thesis (Droogleever Fortuyn, 1911), and will repeat here only the principal points.

As soon as possible after the death of the animal, but in every case within 24 hours, the brain was put into 5 per cent. formalin. When in this fluid, it was drawn as seen laterally and from above, and after having separated the hemispheres from each other and from the cerebellum I made a drawing of the median surface, except in the mouse, the waltzing-mouse and *Dipodomys*, where the brain was treated as a whole. These drawings were very useful for the construction of the maps illustrating this paper.

After some time the pia mater was removed from the brain, for if allowed to remain the hardened blood vessels tend to tear the sections. The brain was then placed into alcohol. Four brains of waltzing-mice presented to me by Dr. Quix were placed direct into alcohol and were never in formalin.

The brain itself was penetrated afterwards with soft paraffin (42° or 45°), but surrounded by a mantle of harder paraffin by embedding it in paraffin at 58°.

The brains were cut into serial sections of 10 micra. If the series were not totally stained (which was only the case with the waltzing-mouse), the sections were counted and one out of 10, 20 or 25 was stained and studied. The remaining sections were kept in due arrangement in sheets of filtering paper, to be

treated later on if necessary. Much time and labour is spared in this way, and only few sections are lost.

The sections were stretched on hot water and stuck on slides in the usual way, but they were dried only for one hour at a temperature of 35°, as they would otherwise be spoiled.

The sections were stained with Nissl-soap-methyleneblue from Grüber.

I never covered the sections with a covering-glass, because this tends to make the sections lose their colour. If the slides are dried on a place free from dust, the balsam forms a smooth and hard surface. The only disadvantage of omitting the covering-glass is the fact that an immersion-lens cannot be used. If necessary it is possible to apply another layer of balsam and cover-glass.

Some series of the waltzing-mouse were stained with Heidenhain's hæmatoxylin in order to have some series which would keep their colour.

At the time the brain was taken out of the skull, the internal ears were separated from the skull and preserved in 5 per cent. formalin. To count the number of cochlear-windings the bulla was opened and then the cochlear windings were counted with a binocular microscope.

The nervus octavus between its entrance in the skull and its entrance in the brain was too short to make it possible to cut a piece of it in order to count the number of fibres in it. So I freed the internal ear from lime in a weak solution of nitric acid in formalin. After the removal of the acid with water the ears were treated with fluorochrome and bichromate of potash and embedded in paraffin. Care was taken to note the exact position of the ear in the block in order to make it possible to cut the nervus cochlearis which runs at the side of the nervus vestibularis quite transversely. In that case the number of fibres in it may be counted most conveniently.

The thickness of the sections in these series was 15 or 20 micra. and they were stained by the Weigert-Pal method.

By means of the "Okular-Netzmikrometer" from Zeiss (a square subdivided into squares), the surface of a transverse section of the cochlear nerve was measured and also the number of fibres per square unit was counted. From these data the total number of fibres was calculated. Of course, care was taken to perform these calculations in those sections where the cochlear nerve had already acquired its total thickness.

It would have been also possible to count the number of fibres in that piece of the octavus which remains united with the medulla oblongata when the brain is taken out of the skull. The advantage of the method followed by me is the great security one has of dealing with the cochlear nerve and with this alone because it can be followed into the cochlea in the series.

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I borrowed the method of representing cortical types from the work of Schuster. So the drawings of cortical types illustrating this paper are all made by means of a camera lucida and the same may be said about the more or less schematic drawings of the sections.

I will explain by an example how the reconstruction-projections or maps were made. Suppose the projection of the cortical areas of a hemisphere on the median plane (the symmetrical plane of the brain) to be desired in order to get a reconstruction of the hemisphere as seen laterally or from the median surface. Then a frontal (or horizontal) series was taken, and of every fiftieth or hundredth section the height was measured by means of an ocular-micro-meter. By the height is meant the length of the projection of the transverse section on a line parallel to the median or flat side of the hemisphere. This height was expressed in m. m. and enlarged a definite number of times, indicated on a sheet of paper divided into squares.

If, when the height of a section is indicated ten times enlarged, care be taken to take also the distance between these height lines ten times larger than the real distance of the measured sections (known expressed in micra.), then in this way a quite proportional periphery of the side-view of a hemisphere can be reconstructed.

The drawings previously made of the brain *in toto* control these reconstructions in an excellent way. Besides the periphery the corpus callosum, the anterior commissure and the principal sulci may be projected and indicated in the reconstruction.

The median and lateral views of a hemisphere necessarily must have the same periphery. If this periphery be first reconstructed after data derived from the lateral side of the hemisphere, and subsequent data derived from the median side, for instance, the projection of the corpus callosum, be drawn in it, then no disturbing errors can arise. So the reconstruction of the median side controls that of the lateral side.

The limits of the cortical areas were likewise projected on the median plane under the microscope and then indicated in the reconstruction.

Where a limit was vague the middle of the transitional area was taken as demarcation-line.

Where the projection of one area (for instance, an area situated at the bottom of a fissure), would overlap the projection of another area, for the sake of clearness only the projection of the externally visible area was indicated. The situation of the other area was only described or indicated in the drawings of sections where such areas are more distinctly seen than projected in the map.

These reconstruction schemes finally allowed the maps illustrating

this paper to be made. Of course, the individual peculiarities have disappeared, but I hope these drawings may serve as an exact map for the species.

The maps published by Brodmann, Schuster, Isenschmid, I. de Vries, &c., are, I presume, mental reconstructions. Without doubt with my method, *i.e.*, by measurements, more exact and more objective maps can be obtained. A disadvantage lies in the fact that some areas are reproduced much shortened and distorted. I think I have overcome the difficulty by giving a dorsal as well as the lateral and mesial views.

To estimate the number of ganglion-cells per cubic unit in the cortex of area *p*, I made use of the "Okular-Netzmikrometer," and counted a number of cells in 10 succeeding sections.

DESCRIPTION OF CORTICAL AREAS.

Sciurus vulgaris (L.).

As the structure of the cortex of the brain is particularly clear in the squirrel I will begin with this animal the descriptive chapter.

The external surface of the brain is smooth; the only fissure is the rhinal. The brain of the squirrel is large as compared with the body, judged by a relative comparison of the brain of the rat to its body.

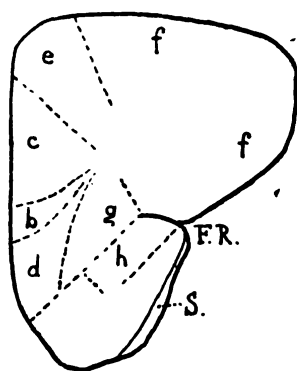


FIG. 1.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag. (See for abbreviations, page 353.)

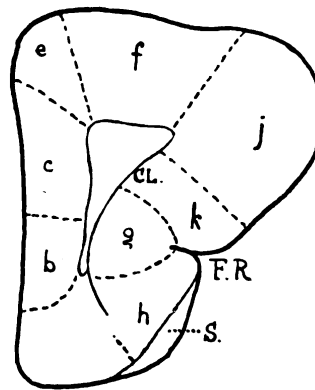


FIG. 2.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag.

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A series of frontal and horizontal sections of the left hemispheres of two squirrel brains were studied with the same results.

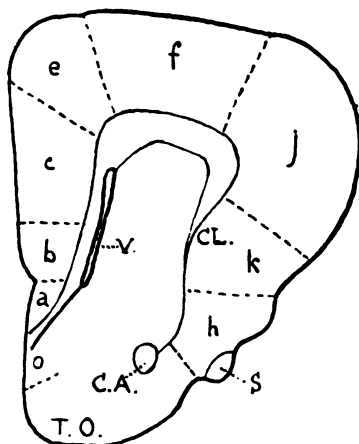


FIG. 3.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag.

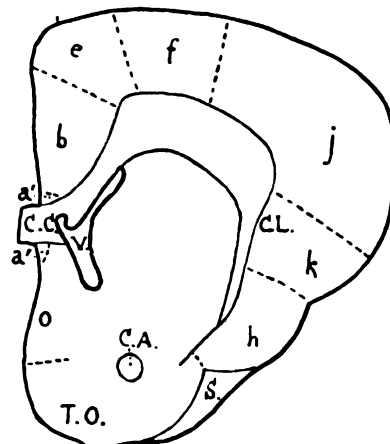


FIG. 4.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag.

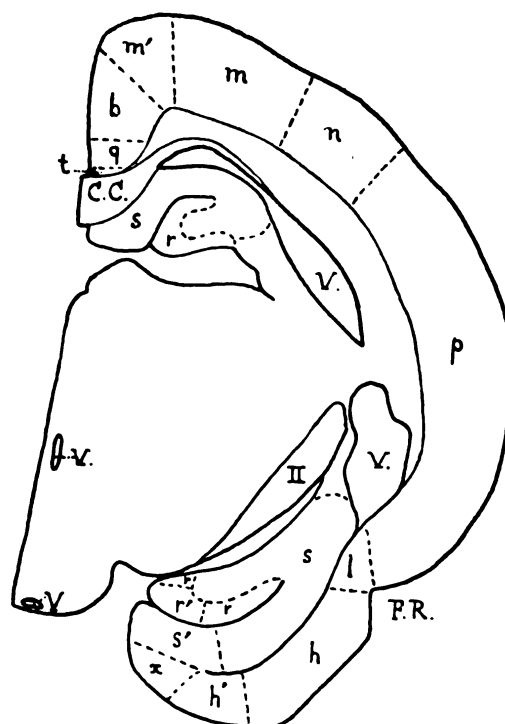


FIG. 5.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag.

If one of the first sections of a frontal series which cut the corpus callosum be taken one gets about the picture of Fig. 4. The corpus callosum pierces the cortex in an area which I will call area a^1 . This area, situated somewhat below and above the corpus callosum, consists of a very deeply staining zonal layer. Beneath this there is a narrow layer of pyramidal cells lying closely together, the lamina pyramidalis or layer III of Brodmann (1909). Under this some large, round inflated granular cells follow, and then a layer of dispersed infra-granular pyramids (layer V). A polymorphous layer (VI) is wanting.

If we follow area a^1 in the other sections we notice it surrounds the fore-part of the corpus callosum. Above this it remains visible more backwards as a narrow border, and at last it disappears even there. Projected on the median plane of the brain, area a^1 has a shape as indicated in Fig. 9, page 233.

Below area a^1 lies an area free from cortex (Figs. 4 and 9), indicated by o as everywhere. It passes into the olfactory tubercle. The cell-lamination of the olfactory tubercle is a very atypical one. I will not describe it anywhere, but only remark, that in rodents two types are mingled. The first type consists only of pyramidal cells, the other type of a layer of granules under an extraordinary narrow zonal layer.

Area a^1 passes forward and down into an area a , being nowhere broad, as Fig. 9 shows, but forming a narrow link from the olfactory tubercle to the genu of the corpus callosum.

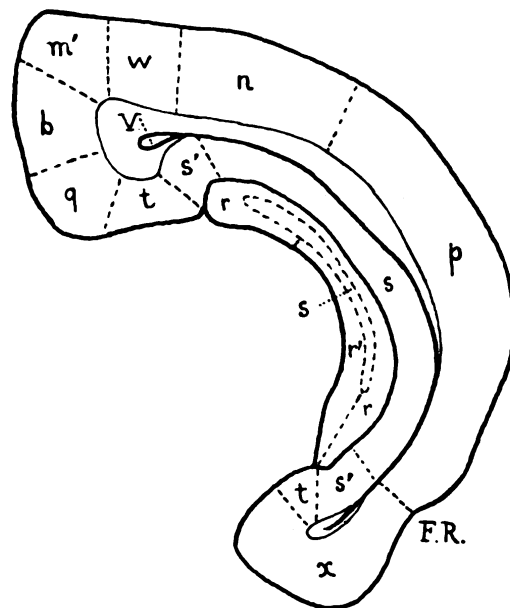


FIG. 6.—*Sciurus vulgaris*. Frontal section of the hemisphere.
Camera lucida drawing. 6 mag.

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The structure of area *a* is very simple, as it consists only of a layer of pyramidal cells under the zonal layer. As the latter one is never absent I shall not mention it regularly in future. The pyramidal layer of area *a* is the lamina ganglionaris, as it is the continuation of layer V of the neighbouring area *b*. Area *a* is limited very indistinctly against the tuberculum olfactorium; the limit of *a* and *b* is a sharp one. Area *a* is visible in Fig. 3.

Area *b* is not only indicated in Figs. 3 and 4 on the median side above area *a* or *a*¹, but also in Figs. 1, 2, 5 and 6, as it is extending far forward and backward. The total extent of it may be seen in Fig. 9. This area has a very remarkable structure (c. o. Plate I, Fig. 1). Immediately below the zonal layer the granular layer (layer IV) is situated, this being very broad and composed of big, inflated cells, fairly round, with a deeply staining nucleus, but a not or hardly staining cell-body. These "inflated granules" resemble glia-cells in some respects, but their body and nucleus is larger, and glia-cells are still so deeply stained that their protoplasm differs not much in colour from the surrounding nerve-fibres.

Under this granular layer is a layer of infra-granular pyramids about equally broad, and beneath this a polymorphous layer (VI) with round and stellate cells, and also with inflated granules. The infra-granular pyramids diminish in size downward. Area *b* has a sharp limit with area *a*, but not with the other neighbouring areas. The transition to these areas, which are all endowed with a layer of supra-granular pyramids, is formed by the highest cells of the granular layer of *b* becoming more deeply stained and assuming now and then the shape of a pyramid. The line, indicating in Fig. 9 the limit of area *b*, runs in the middle of this transitional area.

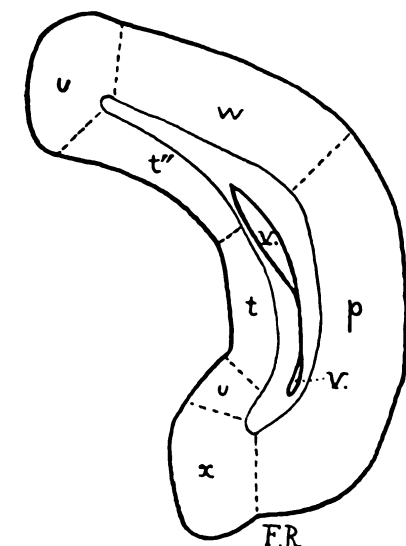


FIG. 7.—*Sciurus vulgaris*. Frontal section of the hemisphere. Camera lucida drawing. 6 mag.

As Figs. 3 and 9 show still another area is present on the median side above and in front of area *b*. It will be indicated with *c*. It is not limited to the median side of the hemisphere, but a point of it bends away in front of the hemisphere, so as to become just visible on the lateral side (Figs. 8 and 12). This part of area *c* turning round may only be recognised in horizontal (or sagittal) sections. In frontal series the cortex of it is too obliquely cut to render its structure recognisable.

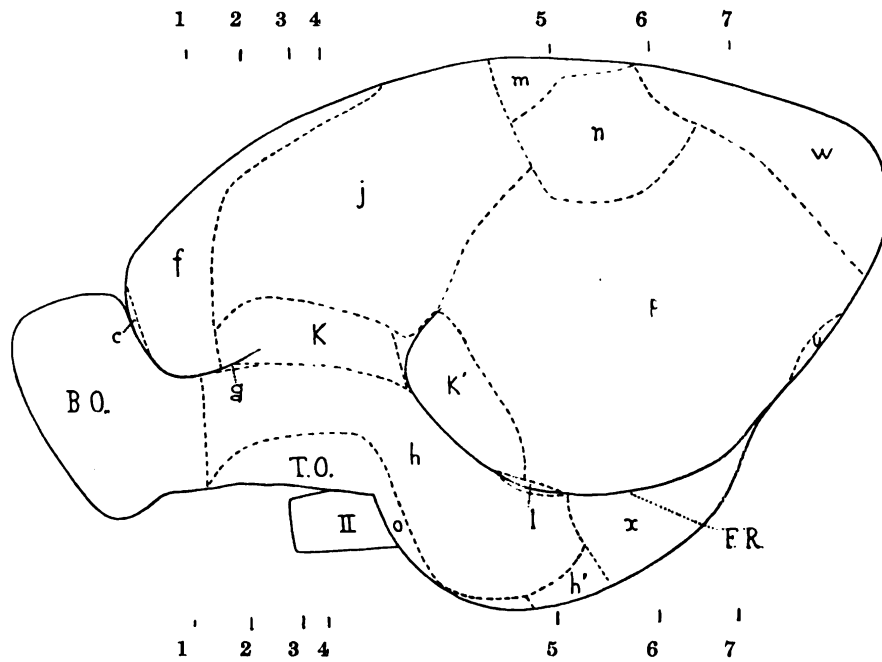


FIG. 8.—*Sciurus vulgaris*. Lateral projection of the hemisphere. 5 mag. The cyphers 1-7 indicate the position of the sections represented by Figs. 1-7. (See for abbreviations, page 353.)

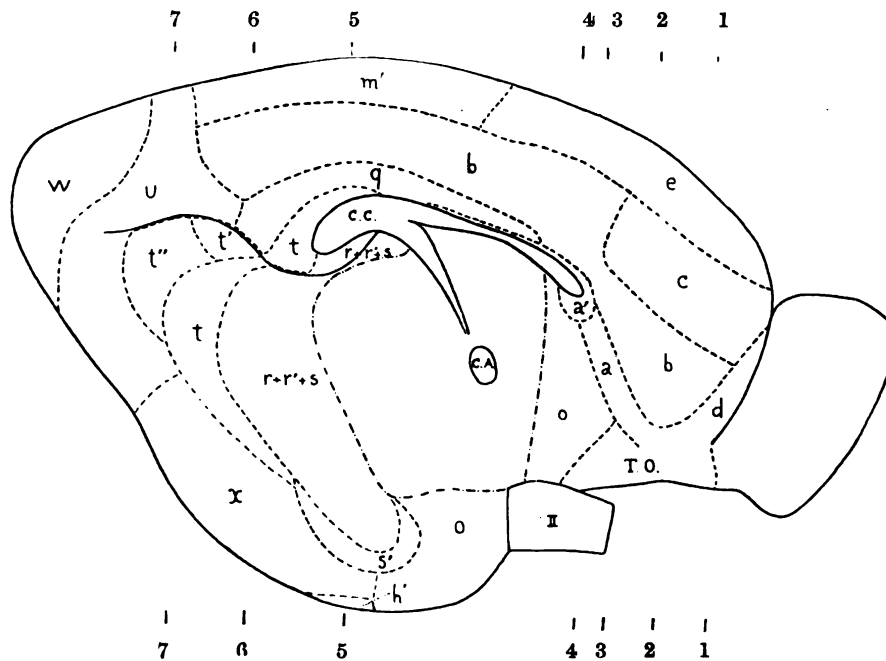


FIG. 9.—*Sciurus vulgaris*. Median projection of the hemisphere. 5 mag.

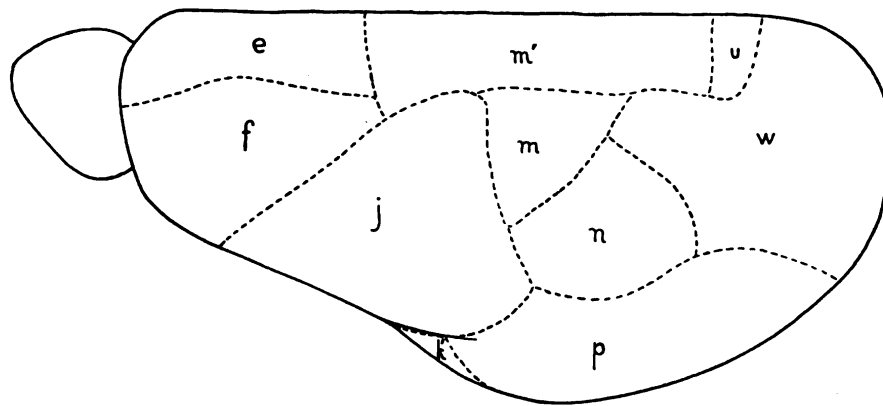


FIG. 10.—*Sciurus vulgaris*. Dorsal projection of the hemisphere. 5 mag.

Area *c* has a layer of supra-granular pyramids (layer III) and a layer of inflated granules, which are together as broad as the granular layer of area *b*. Layers V and VI of area *c* are similarly constructed to those of *b*.

The areas *a*, *b* and *c* show a remarkable structural connection in sections, like Fig. 3, where are included all three. In such sections (confer also on the scheme Fig. 11) we see the breadth of the cortex diminishing from top to bottom. The cortex is apparently pushed away by the corpus striatum

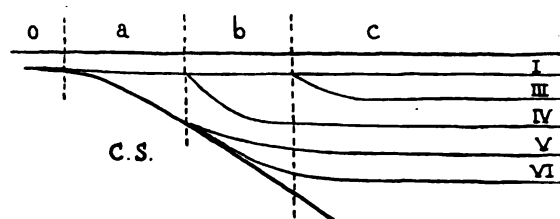


FIG. 11.—*Sciurus vulgaris*. Scheme of the structural connection of the areas *a*, *b* and *c*. I-VI = cortical layers. C.S. = corpus striatum.

which is approaching the surface of the hemisphere below area *a*. As to the cortical layers we see the zonal layer (I) passing uninterruptedly, but the layer of supra-granular pyramids (III) is tapering downward in area *c*, like the layers V and VI. Where layer III is ending the granular layer (IV) lying beneath it, is reaching the surface, and with this area *c* has passed into area *b*. In area *b* the layers IV and VI are tapering. Where they have disappeared only the layer of infra-granular pyramids remains, and with this area *a* appears.

So the corpus striatum, which indeed fills up the place of the cortical layers more and more, seems to push the cortical layers to the surface until they

disappear for want of space. But I do not look upon this as a mechanical explanation of the structure of the areas *a*, *b* and *c*.

In a frontal direction the areas *b* and *c* are bordering upon an area *d* situated at the base of the frontal lobe of the hemisphere (Figs. 1, 9 and 12). It passes gradually into the cortex of the tuberculum olfactorium. A granular layer is missing, consequently it consists only of the layers I, III, V and VI. It is radiating somewhat, *i.e.*, the infra-granular pyramids are much elongated, and are diverging so as to form a fan. This phenomenon is shown also by other areas situated in places where the surface is highly curved and where consequently the section of the area has the shape of a circle-sector. (Fig. 1, area *d*, Fig. 2, area *e*.)

Area *c* and a part of area *b* is on its dorsal side the neighbour of area *e*. It is visible in the projections Figs. 9 and 10, and in the sections Figs. 1, 2, 3 and 4. Area *e* is radiating; layer V is very broad and characterised by large, elongated, deeply staining pyramids. The pyramidal cells which beside cells of all other forms are present in the polymorphous layer, are not less elongated. Layer III consists of distinct, deeply stained pyramids, and is about as broad as layer III of area *c*. On the other hand, layer IV is very narrow, half as broad as III, and it is not built up of granular cells but of very small pyramids. So area *e* is an agranular area.

A large portion of the frontal lobe of the hemisphere is occupied dorsally by area *f*, bordering upon area *e* (Figs. 1, 2, 3, 4, 8 and 10). Area *f* resembles area *e* in some respects, but one can discriminate it from area *e*, as it is not radiating, and because the layer of supra-granular pyramids is twice as broad; moreover, there is an indistinct, narrow granular layer with some small, non-inflated granules. In such non-inflated granules in contradistinction to the inflated ones no difference in the tint of cell-body and nucleus can be seen. The lamina ganglionaris is broad and contains many large pyramids. Layer VI is separated into a layer of small pyramids, below layer V, and a layer of typical polymorphous cells. Area *f* is tapering caudally (Fig. 10).

With area *g* all the areas of the frontal lobe are summed up. Its projection is just visible in Fig. 8, and in Fig 12, where the olfactory bulb is supposed to be cut. Besides, one may see it in Figs. 1 and 2. It occupies together with area *d* the ventral side of the frontal lobe, and it is ending soon behind

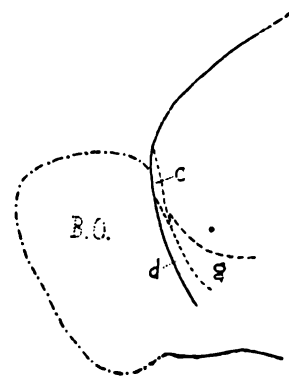


FIG. 12.—*Sciurus vulgaris*. Lateral projection of the frontal pole of the hemisphere. 5 mag. The olfactory bulb (B.O.) is supposed to be cut.

the section presented by Fig. 2. It is characterised by very pale supra-granular pyramids resembling granules. But still, this layer has it cells more deeply stained than layer IV. The layers V and VI are poorly developed, especially where, as in Fig. 2, the area occupies the bottom of a fissure.

In Fig. 1 area *h* is visible already beneath the rhinal fissure. It is also indicated in Figs. 2, 3, 4 and 5, and its projection on a sagittal plain in Fig. 8. Area *h* occupies the whole region below the rhinal fissure, the tuberculum olfactorium excepted. It ends under the temporal lobe. As to its structure it consists of a dense layer of pyramidal or stellate cells, being layer III, under this a layer almost free from cells, but with very few stellate cells, and under this a polymorphous layer.

Besides the areas dealt with, two areas *j* and *k* are visible in Fig. 2 on the lateral side of the hemisphere.

Area *j* is present caudally and laterally of area *f* and it is extending to the caudal half of the hemisphere (Figs. 8, 10, 2, 3, and 4). Here we meet for the first time with an area with a non-homogenous cell-lamination, a structure with considerable local differences. The greater part of area *j* has a layer of supra-granular pyramids about as broad as in area *f*. Below this follows a distinct granular layer more than half as broad as layer III and composed of deeply staining, oval, non-inflated granules. These granules have quite another type than those of area *b*. Below the granular layer is a layer of infra-granular pyramids, about as broad as layer III and more than half as broad as layer V of area *f*. Moreover, the infra-granular pyramids of area *j*, even the largest ones, lying most deeply, are smaller than those of area *f*. Under layer V is a broad polymorphous layer built up of polygonal cells and small pyramids.

Scattered over the area with the just-described structure some spots are found where the granular layer is somewhat narrower and has twice less cells. One of these spots was 2 mill. in length and $1\frac{1}{2}$ mill. broad. In regard to layer IV such a spot resembles more area *f*.

Have we to call each of these spots a different area? No, in my opinion. For one observes that all these spots show the same structure, although they do not cohere and each of them is inclosed by the area *j* rich in granules. Besides their position and number is not constant in all individuals as is necessarily the case with true cortical areas. So I prefer to say that area *j* shows two types of cell-lamination. I propose to call such areas, of which more examples will be found, dimorphous areas. Not in every dimorphous area one type is inclosed by the other one like a group of islands. Often both types reach the limit of the area and are separated by a very fantastical line of demarcation, or one type is forming, moreover, some islands within the other one.

In general I mean by a dimorphous area a cortical area having as a whole a constant position and having constant limits in various individuals, but showing two structural types which are whimsically and in various individuals most differently mingled. Consequently it is impossible to consider both types as by shape and situation constant areas. I could not find the mention of this phenomenon of dimorphy by other authors. The figures 1, 2 and 6 on Plate II are illustrations of dimorphous areas.

Between the areas *j* and *h* the areas *k* and *k'* are lying with the claustrum under them. By their very peculiarly curved surface there is no direction in which they are cut everywhere at the same angle. In consequence of this but also of the proximity of the rhinal fissure the apparent and actual breadth of the layers varies very much, but the claustrum is always a convenient badge. Area *k* consists of a layer III being poor in cells and a layer IV with only few inflated granules, so few that this layer is distinguished by its poverty of cells and contrasts as a light band with the deeply staining layers III and V. (Layer IV in Plate I, Fig. 2, may serve as an example of such a light band.) Below layer IV the small but broad infra-granular pyramids are present, forming a narrow layer V, not broader than layer III. Layer V is followed by a narrow polymorphous layer poor in cells and under it the claustrum, distinctly developed and rich in polygonal and inflated round cells.

Area *k* is visible in Figs. 2, 3 and 4 and its projection in Fig. 8. Area *k'* differs from area *k* by the presence of inflated granules in layer IV. Thus it does no longer contrast as a light band. Area *k'* has been projected in Figs. 8 and 10.

If frontally area *k* was separated from area *h* by the narrow area *g*, caudally this is in a hundred sections the case for area *k'* by area *l*. This area does not occupy much more than the bottom of the rhinal fissure (Figs. 5 and 8), and is consequently twice or three times as narrow as other cortical areas. The lamina pyramidalis is wanting and the inflated granules of layer IV reach the zonal layer. Under layer IV the narrow lamina ganglionaris and multiformis are present. Area *l* ends in a caudal direction at the same level as area *h*, and I scarcely would have dared to consider so small a region as a cortical area of itself if it was not present also in the rat, for instance (compare Fig. 22, page 266).

The transition of area *j* into the areas of the median surface is no longer formed by area *e*, but by area *m'*, an area which may at once be distinguished from *e* by a granular layer. This area is radiating; compared with *j* the layers III and IV have been reduced nearly twice, while the lamina ganglionaris is very broad and its pyramids are elongated. But moreover, it differs from area *j* by the granular layer being chiefly composed of inflated granules. Only on some points the non-inflated granules predominate.

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In this respect it agrees with area *m*, situated backward of area *j*. This area *m* chiefly differs from area *j* by the granular layer being narrow and all its granules being inflated. Perhaps the infra-granular pyramids are more numerous and they are larger in proportion as they lie deeper in the layer. So, area *m'* is only distinguished from area *m* because it is radiating, *i.e.*, because it is situated on a spot where the surface of the brain is highly curved, and by some non-inflated granules at the side of many inflated ones. For this reason I did not indicate it with a letter of its own, but with the accent.

The transition of area *j* into area *m'* is rather regular, because *j* may begin to radiate before the typical granular layer of *m'* has appeared. The areas *m* and *m'* are indicated in Figs. 8, 9, 10, 5 and 6.

Caudally of the areas *j* and *m* and bordering upon them another area, *n*, is present and it generally agrees with *j* and *m* in structure. This area is characterised by the lamina ganglionaris, a layer poor in cells and not supplied with pyramids of all sizes, but with very small or very large ones. The latter are not numerous and they are the largest pyramidal-cells which *Sciurus* has. The polymorphous layer has, as in *j* and *m*, many small pyramids at the side of other-shaped cells. The granular layer has non-inflated cells, less numerous than in area *j*. The lamina pyramidalis has no peculiar characteristics. Figs. 5 and 6 show area *n*, and its extent may be understood from Figs. 8 and 10.

The only area still to be described and not visible as well on the median side of the hemisphere is area *p*. It occupies the whole temporal region (Figs. 5, 6, 7, 8 and 10). This area, figured on Plate II, Fig. 1, is again a dimorphous area, as soon will be seen. Layer III has no peculiarities, differs not much, for instance, from layer III of area *j*. The lamina granularis interna is characterising, and this shows the dimorphy. In some parts of area *p* it is composed of pretty many inflated granules, in other parts of still more numerous but non-inflated granules. If both types of area *p* are mapped, like the other areas, then very whimsical limits appear, varying widely in various individuals. On this account I join both types into one dimorphous area. The extent of area *p* as a whole was practically the same in both my individuals. The breadth of the granular layer seems to be somewhat less in the type with inflated granules, than in the type with non-inflated ones.

Area *p* differs also in layer V from the areas *j* and *n*. There are, namely, more but smaller pyramids than in one of these two areas, and they are more of equal size. Layer VI shows less pyramidal, but on the contrary, more stellate cells than in area *j* or *n*.

Returning in the description of the areas to the median surface of the hemisphere I observe between area *b* and the corpus callosum an area *q* (Fig. 9), which may also be seen in Figs. 5 and 6. Area *q* distinctly differs from *b*

by the possession of a layer of supra-granular pyramids half as broad as the granular layer of *b*. Under this follows an indistinct granular layer with mixed inflated and non-inflated granules. The layers V and VI lying under it do not differ from those of *b*.

The hippocampus is visible in Fig. 5 beneath the corpus callosum and also below the place where the hemisphere is connected with the diencephalon. The hippocampus consists of the fascia dentata and the cornu ammonis, which are very easily recognised by their characteristic structure. The fascia dentata is only composed of a layer of granules (layer IV) with some scattered stellate cells beneath them, the cornu ammonis only of a layer of infra-granular pyramids. The granules as well as the pyramids are crowded together. The fascia dentata is not one area but two, which will be called *r* and *r'*. In area *r* the granules are inflated, but not in area *r'*. The limit between *r* and *r'* is a sharp one. I shall call the cornu ammonis area *s*. The transition into the neighbouring areas is formed by area *s'*, where the pyramidal cells of area *s* become more and more dispersed to pass finally into layer V of that area, which borders upon *s'*.

I hope that Figs. 5 and 6 will sufficiently indicate the situation of these easily recognisable areas. Generally speaking, area *r'* is present at the median side of area *r*. By the fantastical shape of the areas *r*, *r'*, *s* and *s'* and by their being hidden by one another I could not indicate them separately in the projection (Fig. 9). I projected the areas *r*, *r'* and *s* together in one area (*r* + *r'* + *s*). Only a small part of area *s'* could be projected (compare Figs. 5 and 6 with Fig. 9).

Caudally of the hippocampal formation a set of areas is situated which agree in structure, and will be indicated with *t*, *t'* and *t''*.

Area *t* has the largest extent. It embraces the hippocampus like a crescent and also exists as a narrow band above the splenium. It is visible in Figs. 5, 6 and 7, and its projection which here and there, for instance, in Fig. 6, is much shortened, in Fig. 9. Area *t* has a narrow layer III and layer IV. They are together about half as broad as layer IV of area *b*. Layer III, in itself at least twice as broad as the granular layer, consists of extraordinary small supra-granular pyramids, which are closely packed together. In the granular layer inflated and non-inflated granules are mixed. Beneath this layer is a layer of large infra-granular pyramids, widely dispersed. This layer is about one and a half times as broad as layers III and IV together. Lastly, below this there exists a polymorphous layer with deeply staining, polymorphous cells and without inflated cells.

Area *t'*, situated above area *t* (Fig. 9), resembles it in a high degree. It only deviates from *t* in the layer of supra-granular pyramids being reduced to

nearly one row of cells, while underneath it there appears a distinct granular layer with exclusively inflated cells.

In structure but not in position, area t' forms a transition of t into t'' , visible in Figs. 7 and 9. This area wholly lacks layer III. On the other hand layer IV only composed of inflated granules is seen again enlarged; now this layer is about half as broad as the whole cortex. Below the layer of granules is a layer of pretty large, deeply staining infra-granular pyramids and a polymorphous layer with inflated cells in greater depths.

Area t'' resembles in a striking way area b , except that the total breadth of the cortex is less than in area b ; both areas are separated everywhere by interjacent areas. But for this I should not have hesitated to consider them a single area.

Posterior to the areas t , t' , t'' , b and m' area n is situated (Figs. 7, 9 and 10). It differs obviously from the neighbouring areas, but has no characteristics. The layers III and V, which have both about the same breadth, are distinctly developed, and they have layer IV with inflated cells and only half their breadth between them. Beneath the lamina ganglionaris a broad polymorphous layer is present showing inflated cells underneath and small pyramids in the neighbourhood of layer V. The transition of n into b is a rather gradual one, as I have already remarked when describing area b . Area u does not much deviate from m' , but u has more granules and supra-granular pyramids and less infra-granular pyramids. Besides, it is not radiating.

The occipital lobe of the hemisphere is occupied by area w . It is indicated in Figs. 6, 7, 8, 9 and 10, and is remarkable for the extraordinary development of the granular layer. The layer of supra-granular pyramids is perhaps broader than that of area p , otherwise there is nothing noteworthy in its structure. It passes rather gradually into the granular layer, whose breadth can attain more than a quarter of the total thickness of the cortex; this granular layer is remarkably rich in cells. The granules inflated and non-inflated, but there are also some scattered pyramids in it. The layer of infra-granular pyramids are narrower than layer IV and poor in cells, follows the granular layer. Layer VI is narrower than in area p , for instance. The transition of area w , especially of its granular layer, into the neighbouring areas is a rather gradual one.

The area w very probably is homologous with the area striata of Brodmann (1909), and therefore corresponds to the visual cortex. I could not, however, distinguish a line of Gennari.

The description of two areas occupying the lobus piriformis caudally of area h still remains. The first of them belongs by its structure so much to the type of area h that I shall call it h' . Area h' differs from area h by the

layer of supra-granular pyramids (which is broader than in *h*), being interrupted which causes the pyramids to keep crowded together in groups. Moreover, there is in this area a very narrow, but nevertheless, obvious layer of infra-granular pyramids which is wanting in area *h*, except where it passes into *h'*. So the areas *h* and *h'* have no sharp common limit. Area *h'* has like *h* a narrow polymorphous layer, and instead of a granular layer there is a layer with some few scattered pyramidal cells. Area *h'* is visible in Figs. 5, 8 and 9.

Area *h'* forms a local as well as a structural transition of area *h* into area *x*. This area is extensive, as Figs. 5, 6, 7, 8 and 9 demonstrate. It shows a layer of supra-granular pyramids, twice or three times as broad as that layer in area *h*, and sub-divided into two layers III*a* and III*b*. III*a* is narrower than III*b*, and has larger pyramids, which are packed closer together. As the cells of layer III*a* do not resemble granular cells, I am not inclined to call this layer an external granular layer (layer II). Below III*b* follows a narrow layer IV which is poor in cells if not free from them, and it is obvious as a light band in the cortex. (These characters are also to be seen on Plate I, Fig. 2, where a drawing of area *x* of the rabbit is published.) Beneath layer IV the narrow layers V and VI are present, both together not broader than layer III. The lamina ganglionaris has more deeply stained cells than the polymorphous layer, and here they have more distinctly a pyramidal shape.

I will summarise the characterising histological details of the cortical areas in the form of a table for convenience sake. Yet, in doubtful cases I beg the reader to refer to the text.

Sciurus vulgaris.

(Table of characterising histological details.)

Layer.	Breadth.		Cells.	Further Remarks.
I	Area a.	
V	Pyramids	Continuous with V of b.
I	Area a'.	
III	Narrow	Pyramids.	Deeply staining.
IV	Narrow	Inflated granules.	
V	Pyramids	Cells dispersed. IV and V can be pushed aside by the corpus callosum.

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Layer.	Breadth.	Cells.	Further Remarks.
Area b.			
I			
IV	Very broad	Big inflated granules	On the borders of the area a few pyramids. Cells diminishing in size in greater depths.
V	= IV	Pyramids	
VI		Round or stellate cells or inflated granules.	
Area c.			
I			
III	} III + IV = IV of b	Pyramids.	Similar to V of b. Similar to VI of b.
IV		Inflated granules.	
V			
VI			
Area d.			
I			Radiating.
III			
V			
VI			
Area e.			
I			
III	= III of c	Deep pyramids.	The area is radiating and agranular.
IV	= $\frac{1}{2} \times$ III	Very small pyramids.	
V	Very broad	Large, elongated pyramids.	
VI		Polymorphous cells and elongated pyramids.	
Area f.			
I			
III	= $2 \times$ III of e		Small pyramids in the superior parts and polymorphous cells in the inferior parts.
IV	Narrow	Non-inflated granules.	
V	Broad	Large pyramids.	
VI			
Area g.			
I			Poorly developed.
III		Very pale pyramids, resembling granules.	
IV		Paler than those of III.	
V			
VI			
Area h.			
I			Cells crowded together.
III		Pyramids or stellate cells.	
IV		Very few stellate cells.	
VI			

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area h'.</i>			
I	Pyramids crowded together in groups.
III	Broader than III of <i>h</i>	
IV	Few scattered pyramids.	
V	Very narrow....	A division of III into two layers IIIA and IIIB, is sometimes indicated.
VI	Narrow	
<i>Area j.</i>			
I	This area is dimorphous. The other type has a narrower granular layer with twice less cells.
III	= III of <i>f</i>	
IV	= $\frac{1}{2} \times$ III	Deep oval granules.	
V	= III = $\frac{1}{2} \times$ V of <i>f</i>	Smaller than those of <i>f</i> .	
VI	Broad	Polygonal cells and small pyramids.	
<i>Area k.</i>			
I	Poor in cells.
III	
IV	Very few inflated granules.	Contrasting as a light band.
V	Narrow = III	Small but broad.	Poor in cells.
VI	Narrow	
Clastrum....	Polygonal and inflated	Round cells.
<i>Area k'.</i>			
I	Not contrasting as a light band.
III	
IV	Inflated granules	In other characters similar to <i>k</i> .
V	
VI	
Clastrum....	
<i>Area l.</i>			
I	Twice or three times as narrow as other areas.
IV	Inflated granules.	
V	Narrow	
VI	Narrow	
<i>Area m.</i>			
I	Cells larger when they lie deeper.
III	
IV	Narrow	Inflated granules.	In other characters similar to <i>j</i> .
V	
VI	

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area m'.</i>			
I	
III	$\frac{1}{2} \times$ III of <i>j</i>	
IV	$\frac{1}{2} \times$ IV of <i>j</i>	Inflated or non-inflated granules.	
V	Very broad	Elongated pyramids.	
VI	The area is radiating.
<i>Area n.</i>			
I	
III	
IV	Non-inflated granules...	Less cells than in <i>j</i> .
V	Few pyramids, either very small or very large.	Largest pyramids of <i>Sciurus</i> .
VI	Similar to VI of <i>j</i> and <i>m</i> .
<i>Area p.</i>			
I	
III	Similar to III of <i>j</i> .
IV	Many non-inflated or less inflated granules.	Layer IV shows the dimorphy.
V	Smaller than in <i>j</i> or <i>n</i> ...	Cells not much varying in size.
VI	Less pyramidal but more stellate cells than in <i>j</i> or <i>n</i> . This area is dimorphous.
<i>Area q.</i>			
I	
III	$= \frac{1}{2} \times$ IV of <i>b</i>	
IV	Inflated and non-inflated granules.	Indistinct.
V	Similar to V of <i>b</i> .
VI	Similar to VI of <i>b</i> .
<i>Area r.</i>			
I	
IV	Inflated granules	Cells crowded together; some scattered stellate cells beneath IV. This area is fascia dentata.
<i>Area r'.</i>			
I	
IV	Non-inflated granules.	Similar to area <i>r</i> in other respects.
<i>Area s.</i>			
I	
V	Cells crowded together. This area is cornu ammonis.
<i>Area s'.</i>			
I	
V	Pyramids more dispersed than in <i>s</i> .

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area t.</i>			
I
III	Narrow ; $= 2 \times IV$	Very small pyramids	III + IV are about half as broad as IV of <i>b</i> .
IV	Narrow	Inflated and non-inflated granules.
V	Large	Cells widely dispersed.
VI	Deep, non-inflated cells.
<i>Area t'.</i>			
I
III	Very narrow....	Nearly one row of cells.
IV	Only inflated granules.
V
VI	In other respects similar to <i>t</i> .
<i>Area t''.</i>			
I
IV	Half as broad as the whole cortex.	Only inflated granules.
V	Pretty large.
VI	Inflated cells in greater depths.
<i>Area u.</i>			
I
III	As broad as V	More pyramids than in <i>m'</i> .
IV	$= \frac{1}{2} \times V$	More granules than in <i>m'</i> .
V	Less pyramids than in <i>m'</i> .
VI	Broad	Inflated cells underneath.	Small pyramids near V.
<i>Area w.</i>			
I
III	Broader than in <i>p</i>
IV	$\frac{1}{2}$ of the whole cortex	Many inflated and non-inflated granules and some scattered pyramids.
V	Narrower than IV	Few cells.
VI	Narrower than in <i>p</i>
<i>Area x.</i>			
I
IIIa	} Together $2 \times III$ of <i>h</i>	Larger pyramids, packed closer together than in IIIb.
IIIb	Contrasting as a light band.
IV	Narrow	Few or more
V	} Together smaller than III.	Deeper and more pyramidal shaped than in VI.
VI

Lepus cuniculus (L.).

The brain of the rabbit obviously differs in its external shape from that of the squirrel in the fact that the rhinal fissure (F. R., Figs. 13 and 14) is better

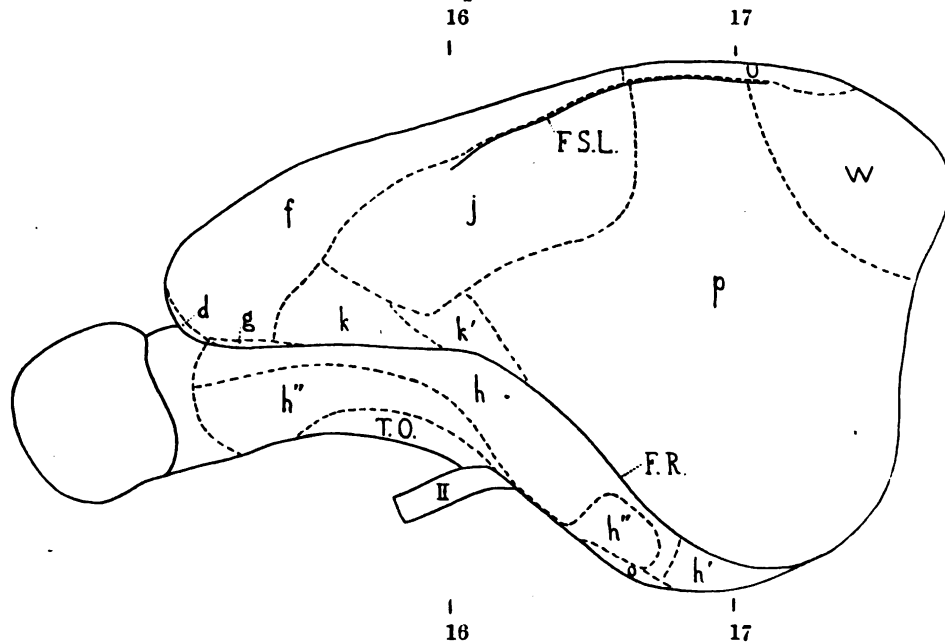


FIG. 13.—*Lepus cuniculus*. Lateral projection of the hemisphere 4 mag. The cyphers 16 and 17 indicate the level of the sections represented by Figs. 16 and 17.

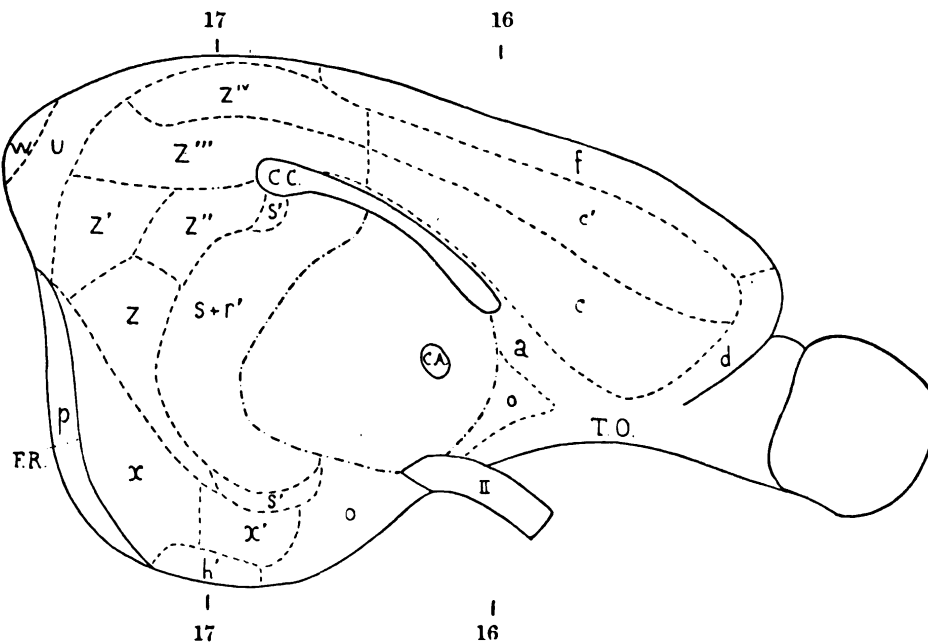


FIG. 14.—*Lepus cuniculus*. Median projection of the hemisphere. 4 mag.

dorsally in the hemisphere, viz., the sagittal lateral fissure (F. S. L., Figs. 13 and 15).

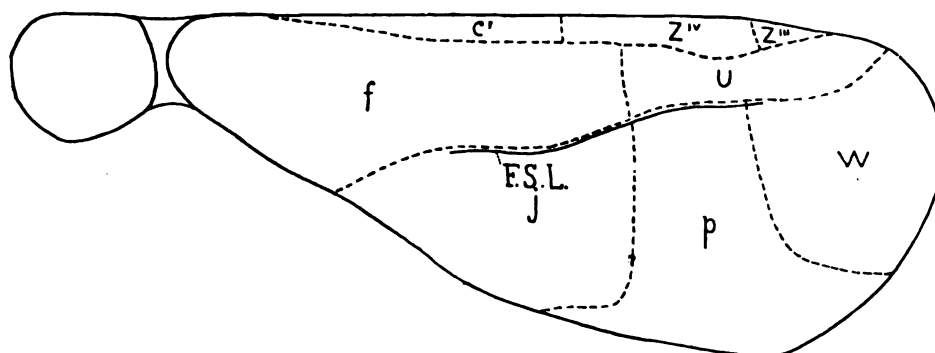


FIG. 15.—*Lepus cuniculus*. Dorsal projection of the hemisphere. 4 mag.

Two serial sections of the rabbit were studied, a frontal one of the left hemisphere, and a horizontal one of the right hemisphere of the same individual.

If again one begins with a frontal section through the fore-end of the corpus callosum (Fig. 16), one does not obtain the same picture as occurs in *Sciurus*.

Just above and below the corpus callosum an area may be observed, which consists only of a layer of infragranular pyramids, and so must be called area *a*. Having made the reconstruction of the projection on the median plane (Fig. 14) one observes that area *a* soon ends below the corpus callosum. Above this, however, it proceeds backward as a narrow band, and in a frontal direction, somewhat enlarged, it joins the olfactory tubercle (T.O.), passing into its cortex without an obvious limit.

So area *a* in *Lepus cuniculus* occupies the place of the areas *a* and *a'* in *Sciurus*. But it has everywhere the structure of *a*. Close to the genu the deepest cells of the pyramidal layer assume a rounder shape, so as to resemble cells of the polymorphous layer, but nevertheless, I could not trace the limits of an area *a''*, as in *Mus decumanus* (Fig. 19, page 261).

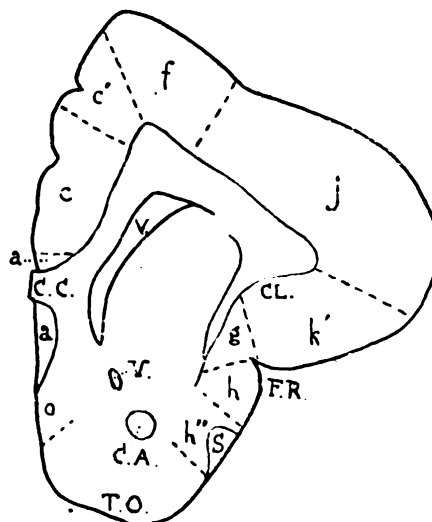


FIG. 16.—*Lepus cuniculus*. Frontal section of the hemisphere. 6 mag. Camera lucida drawing.

In the rabbit an area *b*, i.e., an area where the internal granular layer reaches the zonal layer, does not exist. It will be obvious that the elimination of so large an area (compare *Sciurus*) produces important differences between the maps of the squirrel and the rabbit.

The area which one observes in Fig. 16 above area *a* shows clearly the layers I, III, IV, V and VI. The supra- and infra-granular pyramids here have a peculiar structure. Instead of possessing an obviously pyramidal shape with many dendrites, and instead of staining deeply with Nissl's methyleneblue, their shape is rounded and oval with one or two short dendrites, and they stain palely. Their tint is paler than that of typical pyramidal cells, but deeper than that of inflated granules. These, moreover, differ from them by their circular shape and the want of visible dendrites. As the cells appear to be inflated I shall allude to them as inflated pyramids.

We shall meet this kind of pyramids still in other areas and in other animals. Especially in the guinea-pig, the rat and the mouse. Sometimes, but rarely, in an area with typical pyramids suddenly a group of inflated pyramids or the reverse is seen. But it often occurs that a whole area has inflated pyramids in one series and non-inflated pyramids in another one.

Yet, the preservation is certainly not the only cause of the inflation of the pyramids. In the first place, some areas (areas *f* and *d*) exist which do not show inflated pyramids in any one of my series, and further, generally the areas have only inflated or only typical pyramids. Thus, for instance, where a layer of inflated pyramids passes into a layer of typical ones, the granular layer also changes its characters. Finally, I observed some areas never possessing other pyramids than inflated ones.

To obtain an idea of the shape of these inflated pyramids I refer to Plate II, Fig. 2, where area *p* of the rabbit is drawn. The right half of the figure shows inflated, the left half typical pyramids. The inflated pyramids have a paler tint than the typical ones. This could not be expressed in my drawings, where the tint of the cells has never been indicated. Nay, even here the inflated pyramids by their greater bulk seem to be stained more deeply than the typical pyramids.

Area *c*, situated above area *a*, has a lamina pyramidalis of inflated pyramids about twice as broad as the granular layer, which is built up of inflated and non-inflated granules. The layers V and VI are about equally broad. Layer V consists of inflated pyramids which without doubt are stained more deeply than the supra-granular pyramids. They sometimes rather resemble typical pyramids. The polymorphous layer consists of rounded and rather pale cells, with cells of other shapes between them.

Above area *c* an area is present (*c'*, Figs. 14, 15 and 16), which resembles

c very much in structure and extent, and which therefore will be indicated with *c'*. As in this area the inflated supra- and infra-granular pyramids are extraordinary pale, the layers can scarcely be distinguished. The layers V and VI imperceptibly pass into one another. The granular layer with its inflated granules still has the palest tint.

Besides, area *c'* is characterised by peculiar stripes. Transversally through all layers white fibres are running, which contrast with the back-ground of a very pale-blue tint in my preparations. These fibres proceed from layer VI and continue their way into the lamina zonalis. Area *c* does not show these stripes, or less than other areas, for instance, the areas *c* and *c'* may differ considerably in the mutual relation of their extent. But together they are occupying a constant region, extending backward to the middle of the corpus callosum and forward to the olfactory tubercle. They are precisely limited everywhere (Fig. 14).

In spite of the differences in structure and extent, I consider *c* and *c'* the homologues of area *c* in *Sciurus*.

Area *c* does not turn round the hemisphere to its lateral side, as it did in *Sciurus*. Frontally on the median side it borders upon area *d* (Figs. 13 and 14), which occupies, as in *Sciurus*, the ventro-median part of the frontal lobe of the hemisphere, without being separated from the cortex of the olfactory tubercle. As in *Sciurus* it is radiating, has deeply stained, non-inflated supra- and infra-granular pyramids and a polymorphous layer of inflated cells. It is not quite agranular. Between the layers III and V lies a very narrow granular layer with some non-inflated granules.

Immediately above area *c'* area *f* is situated (Figs. 14 and 16). Once more this area occupies a large portion of the frontal lobe and it tapers backward (Figs. 13 and 15). A part of it (the one which is visible in Fig. 14) is radiating. But this is only expressed by the elongation of the infra-granular pyramids, and it did not induce me to call this radiating portion area *f'*. *Lepus cuniculus* lacks area *e* of *Sciurus*.

Area *f* in the rabbit is dimorphous. The greater part of the area is composed of a layer of deeply stained, typical supra-granular pyramids above a distinct granular layer, half as broad and consisting of inflated and non-inflated granules. Below this follows the layer of infra-granular pyramids, deeply stained and non-inflated, but with many inflated cells (inflated pyramids?) between them. Of similar pale-tinted, rounded cells also layer VI is built up, at least the superior part of it. Very deep in the cortex close to the myelum is a narrow layer of deeply stained polymorphous cells.

The layers III and VI have not changed but the granular layer is replaced by a layer of very small, but distinct pyramids. In the lamina ganglionaris

Area *g* consists of inflated supra-granular pyramids, a granular layer extremely poor in cells, inflated, but sometimes rather deeply-stained infra-granular pyramids and a polymorphous layer of pale tinted cells. It has a very compact structure.

Below the rhinal fissure the area is existing which agrees with area *h* in *Sciurus*. Here, however, it has not the same structure everywhere. A part of it lying close to the rhinal fissure (Figs. 13, 16 and 17, *h*) has typical, deeply-stained pyramids; the other part, situated beneath the olfactory tract (Figs. 13 and 16 *h'*), consists of inflated pyramids. Both parts extend below the temporal lobe. As *h* and *h'* were nearly symmetrically situated in both hemispheres, I made two areas of them. It remains possible that area *h* must be called a dimorphous area, but in that case it is a dimorphous area, with transitional regions where some typical pyramids are scattered among the inflated ones. Area *h'* borders upon the olfactory tubercle and more caudally upon a region *o* free from cortex.

As a transition of the areas *h* and *h'* into area *x* a small area *h'* is existing, demonstrated by Figs. 13, 14 and 17. It is chiefly composed of inflated pyramids, but for the rest it has the characters of *h'* in *Sciurus*, viz., a broad, discontinuous layer of supra-granular pyramids, and an extremely indistinct layer of infra-granular pyramids. Layer III sometimes is divided into two layers, the one above the other. In that case the superior one, III^a, is composed of groups of typical pyramids, the inferior one, III^b, of groups of inflated pyramids. A similar division was indicated in *Sciurus* already.

As before, area *j* is situated laterally from area *f*. No dimorphy, as in *Sciurus*, could be perceived in the rabbit. The area has been projected in Figs. 13 and 15, and also Fig. 16 shows it. Just as *j* in *Sciurus*, it is distinguished by very numerous granules (inflated granules and other ones), which are crowded together in a broad layer. It may be most conveniently distinguished from the areas *f* and *p* by its many granules. Layer III does not differ from that layer in *f*, except there are somewhat more and somewhat smaller typical pyramids than in *f*, but besides there are also many inflated pyramids.

Area *k*, with the claustrum, borders upon the ventral side of area *j* as Fig. 13 shows. It consists of a layer of inflated supra-granular pyramids which are more or less grouped, as in area *h'*. Beneath this layer is a layer IV, poor in cells and contrasting as a light band. Then there comes a broad layer of inflated infragranular pyramids, among which some typical pyramids are dispersed. Between the layers V and VI a narrow layer poor in cells is existing, which again contrasts with its environs as a light band. The polymorphous layer itself is only composed of inflated cells, being a trifle paler in tint than the inflated cells which form the claustrum.

More caudally the claustrum is covered by an area which deviates in some respects from *k* by its structure, and which will be called *k'* (Figs. 13 and 16).

The principal difference from *k* is the fact that layer IV has a great number of granules, consequently no longer contrasts as a light band. The cells of layer IV are only partly inflated granules. Between them are many cells resembling inflated pyramids. The narrow light band between V and VI has also disappeared in *k'*. Without regard to the claustrum, *k'* agrees in its structure rather well with the neighbouring area *p*. The conformity of the areas *k* and *k'* with those of *Sciurus* is striking.

The extremely large area *p*, which succeeds the areas *j* and *k'* in a caudal direction, is dimorphous, as it was in *Sciurus*. One type (Plate II, Fig. 2, to the left) has a lamina pyramidalis of typical pyramids above a granular layer of inflated and non-inflated granules half as broad. In this layer IV the cell-density is less than in the areas *j* or *w*; the layer itself, too, is narrower. Layer V is broader than layer IV. Pretty many typical, deeply-stained, pyramidal cells are present in it, but very few cells of other shapes are between them. This layer, therefore, is remarkable in poverty in cells, and there is even an indication of a pale band free from cells between layers V and VI, just as I observed in *k*, where the phenomenon was more obvious. Layer V shows striae like those observed in area *c'*. Beneath the lamina ganglionaris the polymorphous layer is present, consisting of rather deeply-stained cells of various shapes, but not divided into two layers as in the areas *j* and *f*.

The other type of area *p* (Plate II, Fig. 2, to the right) is fantastically mixed with the first type. As a rule all the pyramids of the supra-granular layer are inflated, but in layer V often a few typical pyramids are left. The result of the inflation of the pyramids is this, that the layers III, IV and V can hardly be discriminated. Layer V remains poor in cells, and by this it can be well discerned from layer VI. The stripes, which in the first type were only visible in layer V, can now often be seen in all layers.

This type of area *p* reminds us of area *c'*, with which, of course, it has nothing to do.

I figured area *p* in the Figs. 13, 15 and 17, but also in Fig. 14, as it is approaching the rhinal fissure and visible on the mesial surface.

Area *p* is separated from area *g*, which occupies the bottom of the rhinal fissure by a narrow area *y*. It begins shortly in front of Fig. 17, where it is visible, and follows the rhinal fissure to the end. In the way followed by me it cannot be projected anywhere, and so it is not indicated in Figs. 13 and 14. The area has a broad lamina pyramidalis with typical and never inflated pyramids. There is no granular layer in it, but a narrow lamina ganglionaris with large, non-inflated pyramids, somewhat larger than the supra-granular

pyramids. Besides there is a polymorphous layer of inflated cells. Area *y* everywhere occupies the place which it is occupying in Fig. 17, and never has a larger extent. It does not occur in *Sciurus*.

Area *w* is occupying the occipital lobe of the hemisphere, and so it is demonstrated by Figs. 13, 14 and 15. Generally speaking, it agrees in structure with area *p*. There is a layer of supra-granular pyramids of the usual breadth, the cells of which may be more or less inflated. Yet this is not the cause of an obvious dimorphy. The granular layer is extraordinary broad, more than half as broad as layer III and rich in inflated and non-inflated granules. Moreover, remarkably many deeply-stained pyramids are dispersed in it. They give me the impression of having wandered from layer V. At the side of typical pyramids there are many inflated cells in layer V, but, as in area *p*, a narrow layer poor in cells is present between V and VI. The polymorphous layer does not differ from that layer in area *p*.

For a great distance area *w* borders upon an area which is occupying about the place of the areas *m*, *m'* and *u* of *Sciurus*, but which I will call *u* on account of its position. In structure it agrees more with *m* and *m'* than with *u*. Laterally area *u* extends towards the fissure sagittalis lateralis, but it never reaches the bottom of it (Fig. 17). So it has the limits which Figs. 13, 14 and 15 show. As to its structure, it is composed of a layer of typical or inflated supra-granular pyramids, less than half as broad as layer III in area *w*. Beneath this follows a narrow layer of small, scarcely inflated granules and then an extraordinary broad and often radiating layer of typical infra-granular pyramids. This lamina ganglionaris is about twice as broad as in *p* and *w*. No poverty in cells can be observed, and layer V immediately joins a polymorphous layer as broad as it. This consists as usual of inflated cells, but distinct pyramidal cells are mixed with them. A narrow strip of area *u*, lying closely to the sagittal lateral fissure is more clearly radiating and shows more supra- and infra-granular pyramids and fewer granules than the rest of the area. It seems to be a transitional region formed by the influence of the fissure. Compare also *Lepus europaeus*, page 291.

The description of some areas on the median side of the hemisphere still remains.

Some of them are directly comparable with areas in *Sciurus*. Thus, for instance, area *x*, which borders upon the rhinal fissure and is obvious by a light band, viz., the granular layer free from cells. Above layer IV a broad layer III is present, which again may be divided into two layers: III^a with large and deeply-stained pyramids, and III^b with small pyramids, which are more dispersed. Below the granular layer perhaps some few stellate cells are representing the infra-granular pyramids. Undermost is a polymorphous

layer with deeply-stained cells at the side of pale, inflated ones. Layer VI is narrower than layer III. I reproduced in Plate I, Fig. 2, a drawing of area x .

In a frontal direction x passes into area x' (Fig. 14), which has the structure of x , but all cells are inflated, and there are some inflated granules in layer IV. Consequently it is poor in cells but not free from them.

The fascia dentata and cornu ammonis agree with what I found in *Sciurus*. Again I project them together (Fig. 14, $r' + s$) on account of the obstacles which their separate projection would meet. The dentate fascia (r') is formed by a very narrow layer of stellate cells being crowded together. In some spots the cells are paler and rounder than elsewhere, but they are never truly inflated granules, as in *Sciurus*. They resemble more inflated pyramids. Below the granular layer of r' a layer of scattered stellate cells is present. Area s , the cornu ammonis, consists of distinct, deeply stained pyramids or of inflated pyramids. I could not divide either r' or s into two separate areas (as r and r' in *Sciurus*).

As in *Sciurus*, area s is accompanied by a transitional region s' into the neighbouring areas. Here the pyramids are more and more dispersed to pass finally into the infra-granular pyramids of the neighbouring area. Only a part of area s' can be projected (Fig. 14), but together with s and r' it is visible in Fig. 17.

A group of areas with allied structures surround the hippocampal formation and the splenium like a crescent. They agree with the group of t -areas (t , t' and t'') in *Sciurus*; yet, I am not able to homologise any one of them with a t -area either on account of a different structure or on account of a different situation. So I will call them the group of z -areas (Figs. 14 and 17, areas z , z' , z'' , z''' and z'''').

Area z , which is occupying a part of the place of t in *Sciurus*, is an agranular area. It consists of a layer of deeply-stained, supra-granular pyramids, being very small and very closely crowded together. This layer lies immediately above a layer V. It is three to four times as broad, and its pyramids are small indeed, but they are more dispersed. Undermost lies a narrow polymorphous layer with rather pale cells. In some spots the limit between the layers V and VI is especially distinguished by a narrow strip poor in cells and contrasting as a light line in the cortex. An area of similar structure is lacking in *Sciurus*.

Above area z two areas are present. The posterior one, area z' , has a complete cortex. Beneath a narrow layer of deeply-stained supra-granular pyramids is an obvious granular layer with many non-inflated granules. Then follows the lamina ganglionaris, broader than III and IV together, with rather large, widely dispersed, deeply-stained pyramids. Some inflated cells are

scattered among them. Finally, there is a layer VI as broad as the granular layer, and composed of pale-tinted cells of various shapes. By its structure this area z' resembles area t' of *Sciurus*. Its position, however, is quite a different one.

Area z'' is distinguished from both former area, because it lacks layer III. Consequently the non-inflated granules are lying closely to layer I. Their density is somewhat greater in the neighbourhood of the zonal layer than on greater depth in the cortex. Below the granules is a layer of infra-granular pyramids. These are deeply stained and rather large, and they are not dispersed. The layers IV and V are about of equal breadth. Layer VI is only represented by some few cells. By the want of layer III, area z'' reminds one of area t'' of *Sciurus*, but its situation is different. The transition of z' into z'' is a rather gradual one.

There is an area z''' above z'' . It possesses a narrow layer of inflated supra-granular pyramids above a granular layer twice or three times as broad. The non-inflated granules of the latter are more packed together as they approach layer III. The ganglionic layer under it is rather broad. Its cells, inflated pyramids and some non-inflated ones, are widely dispersed. The polymorphous layer under it consists of pale round cells. The structure of z''' agrees most of all with that of t in *Sciurus*.

Lastly, above area z''' , area z^{iv} is situated. The latter resembles the former in some respects, but it can be distinguished from it by its granular layer being as broad as the layer of inflated supra-granular pyramids and being composed of inflated granules. Moreover, the deeply-stained pyramids in layer V are nearly totally absent. In other respects the layers V and VI agree with those of area z''' .

The areas z''' and z^{iv} show the peculiar stripes found in area c' . They are also the continuation of the areas c and c' .

The regions which are free from cortex and the place where the hemisphere is connected with the other portions of the brain take about the same position as they did in *Sciurus*.

Lepus cuniculus.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
I	
V	Inferior cells rounder in shape.
(16147)			x 2

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area c.</i>			
I	
III	2 × IV	Inflated pyramids.	
IV	
V	As broad as VI	Inflated pyramids	Cells deeper stained than those of III.
VI	Rounded, rather pale.	
<i>Area c'.</i>			
I	
III	Extraordinary pale.	
IV	Palest cells of all.	
V	Extraordinary pale.	
VI	Much resembling area c. White fibres across all layers.
<i>Area d.</i>			
I	
III	Non-inflated pyramids.	
IV	Very narrow	Non-inflated granules.	
V	Non-inflated pyramids.	
VI	Inflated cells.	The area is radiating.
<i>Area f.</i>			
I	
III	Typical pyramids.	
IV	$\frac{1}{2} \times$ III	Inflated and non-inflated granules.	
V	Non-inflated pyramids	With many inflated cells between them.
VI	Inflated, rounded cells	Close to the myelum a narrow layer of deep polymorphous cells. This area is dimorphous. In the other type IV consists of small pyramids and V contains more pyramids and less inflated cells
<i>Area g.</i>			
I	
III	Inflated pyramids.	
IV	Very few cells.
V	Inflated pyramids	Pyramids rather deeply stained.
VI	Pale cells.	This area has a very compact structure.
<i>Area h.</i>			
I	
III	Typical, deep pyramids	
IV	Very few, stellate cells.	Cells crowded together.
VI	
<i>Area h'.</i>			
I	
III _A	Typical pyramids	Cells grouped } These layers are sometimes united.
III _B	Inflated pyramids	
IV	Few scattered pyramids.	
V	Very narrow	Very indistinct.
VI	Narrow	

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area h'.</i>			
I	
III	Inflated pyramids.	
IV	
VI	Similar to <i>h</i> in other respects.
<i>Area j.</i>			
I	
III	Similar to III of <i>j</i> .
IV	Broad	Inflated and non-inflated.	Extraordinary many granules.
V	Inflated and non-inflated pyramids.	More and smaller pyramids than in <i>j</i> .
VI	Similar to VI of <i>j</i> .
<i>Area k.</i>			
I	
III	Inflated pyramids	Pyramids more or less grouped.
IV	Poor in cells; forming a light band.
V	Broad	Inflated pyramids	Some typical pyramids between the inflated ones.
VI	Inflated cells	Cells paler than those of the claustrum.
Clastrum....	Inflated cells.	Between layers V and VI is a narrow layer, poor in cells, contrasting as a light band.
<i>Area k'.</i>			
I	
III	
IV	Many inflated granules	Not contrasting as a light band.
V	
VI	
Clastrum....	No light band between V and VI. Similar to <i>k</i> in other respects.
<i>Area p.</i>			
I	
III	Typical pyramids.	
IV	$\frac{1}{2} \times$ III	Inflated and non-inflated granules.	Less cells than in <i>j</i> or <i>w</i> .
V	Broader than IV	Typical pyramids	Few cells of other shapes between the pyramids.
VI	Deep polymorphous cells.	Not divided into two layers.
A narrow band, free from cells, is indicated between V and VI. Layer V shows such stripes as <i>c'</i> demonstrates. This area is dimorphous. In the other type all the pyramids are inflated except some pyramids of layer V. Transversal stripes in all layers.			

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area r'.</i>			
I
IV	Very narrow....	Stellate or round cells....	Cells crowded together, some scattered; stellate cells beneath IV. This area is fascia dentata.
<i>Area s.</i>			
I
V	Narrow	Deep or inflated pyramids.	Cells crowded together. This area is cornu ammonis.
<i>Area s'.</i>			
I
V	Pyramids more dispersed than in <i>s</i> .
<i>Area u.</i>			
I
III	$\frac{1}{2} \times$ III of <i>w</i>	Inflated or typical pyramids.
IV	Narrow	Small granules.
V	Very broad, $2 \times$ V of <i>p</i> or <i>w</i> .	Typical pyramids	No poverty in cells; often radiating.
VI	As broad as V	Inflated cells and pyramids.
<i>Area w.</i>			
I
III	More or less inflated pyramids.
IV	Very broad, more than $\frac{1}{2} \times$ III.	Inflated and non-inflated granules.	Rich in cells, many deep pyramids dispersed in it.
V	Typical pyramids and inflated cells.
VI	Similar to VI of <i>p</i> . Between V and VI in a narrow layer, poor in cells.
<i>Area x.</i>			
I
III _A	Large, deep pyramids.
III _B	Small, dispersed pyramids.
IV	This layer is free from cells; light band.
VI	Narrower than III	Inflated cells and deep cells.	Layer V is perhaps represented by some few stellate cells.
<i>Area x'.</i>			
I
III _A	Inflated pyramids.
III _B	Inflated pyramids.
IV	Some inflated granules.
VI	Inflated cells.	In other characters similar to <i>x</i> .

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area y.</i>			
I	
III	Broad	Typical pyramids	Pyramids never inflated.
V	Narrow	Large, typical pyramids.	
VI	Inflated cells.	The area is agranular.
<i>Area z.</i>			
I	
III	Very small, deep pyramids.	Pyramids crowded together.
V	4 × III	Small pyramids	Pyramids more dispersed than in III.
VI	Rather pale cells.	Layers V and VI are separated by a light line; agranular area.
<i>Area z'.</i>			
I	
III	Narrow	Deep pyramids.	
IV	Many non-inflated granules.	
V	Broader than III + IV.	Large, deep pyramids....	Pyramids widely dispersed.
VI	= IV	Pale cells of various shapes.	
<i>Area z''.</i>			
I	
IV	Non-inflated granules....	Cells more crowded together near I.
V	= IV....	Deep, rather large pyramids.	Cells not dispersed.
VI	Only few cells.
<i>Area z'''.</i>			
I	
III	Narrow	Inflated pyramids	
IV	2 or 3 × III....	Non-inflated granules....	Cells more crowded together near III.
V	Broad	Inflated pyramids	Cells widely dispersed; some non-inflated pyramids.
VI	Pale, round cells.	The area shows transversal white stripes.
<i>Area z'v.</i>			
I	
III	Inflated pyramids.	
IV	= III	Inflated granules.	
V	Only inflated pyramids	In other respects similar to V of z'''.
VI	Similar to VI of z'''. The area shows transversal white stripes.

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Mus decumanus (Pall.).

The brain of the rat is much smaller than that of the rabbit or of the squirrel. The rhinal fissure (Fig. 18, F.R.) is the only fissure, but it is distinctly visible.

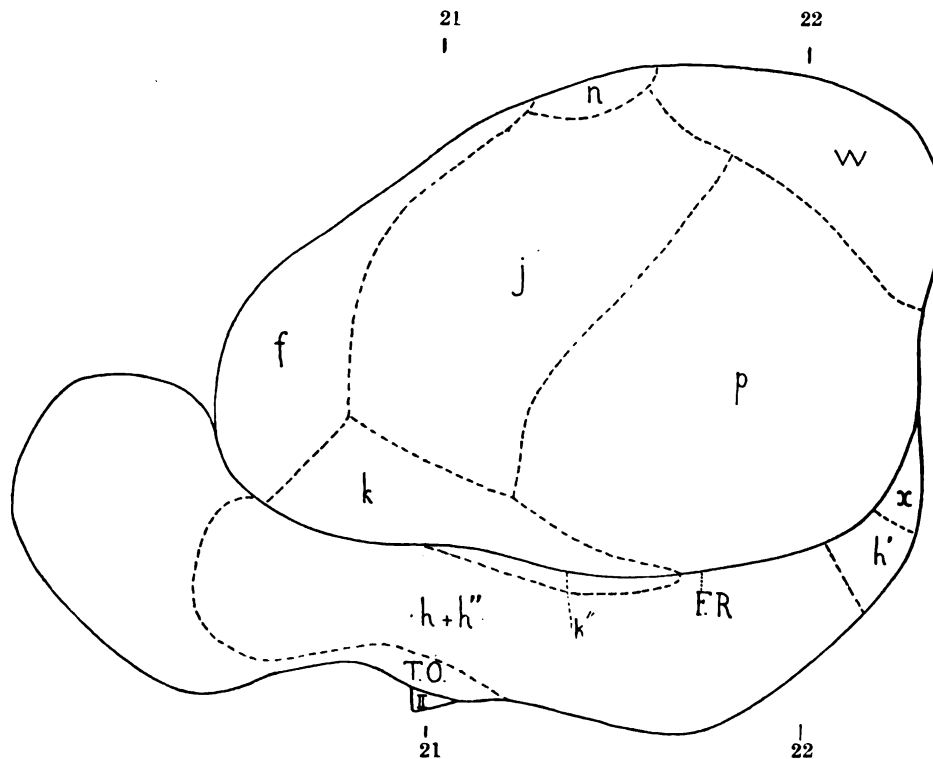


FIG. 18.—*Mus decumanus*. Lateral projection of the hemisphere. 10 mag. The cyphers 21 and 22 indicate the level of the sections represented by Figs. 21 and 22.

Three serial sections of the rat were studied, a frontal one of the left hemisphere and a horizontal one of the right hemisphere of the same individual, and moreover, a series of frontal sections of the left hemisphere of another individual.

Let me commence the description of the cortical areas by the area which is surrounding the genu of the corpus callosum. It is again area *a'* found by me in *Sciurus*. It has a complete cortex, i.e., a cortex in which all layers are present, but its structure is very compact, and immediately near the corpus callosum the layers V and VI may be totally pushed away. The area may be

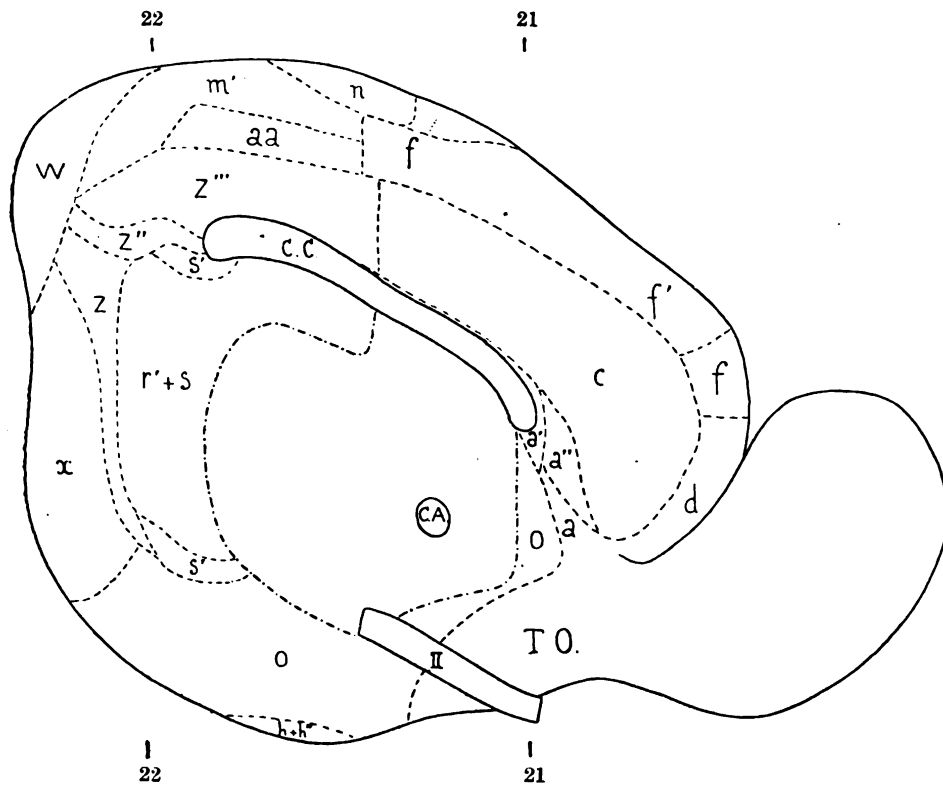


FIG. 19.—*Mus decumanus*. Median projection of the hemisphere. 10 mag.

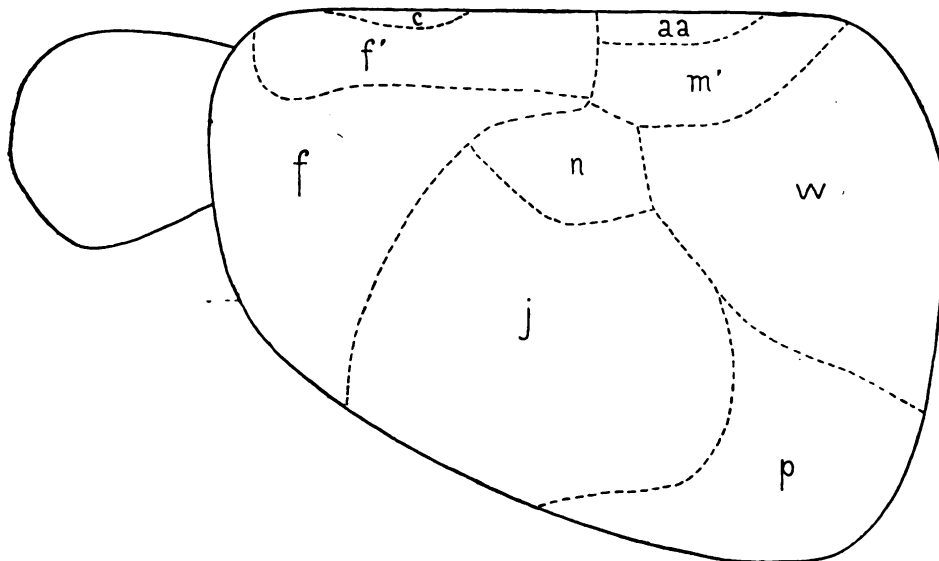


FIG. 20.—*Mus decumanus*. Dorsal projection of the hemisphere. 10 mag.

recognised everywhere by the deep stain of the zonal layer. Its structure can be best observed near the limit of *a''*. There one observes below the zonal layer a narrow layer of crowded pyramids and underneath a layer of inflated granules. The layers V and VI have about an equal breadth. The former consists of inflated pyramids, the latter chiefly of inflated, very pale cells.

Area *a'* is indicated in Figs. 19 and 21. In a frontal direction it passes into an area *a''* with a new structural type. Indeed it only consists of the layers V and VI. The polymorphous layer does not differ from that layer in area *a'*; the lamina ganglionaris is about one and a half times as broad. As its pyramids are inflated, it is in clear contradistinction with area *a*, which, as usual, is only composed of a ganglionic layer of true, deeply-stained pyramids.

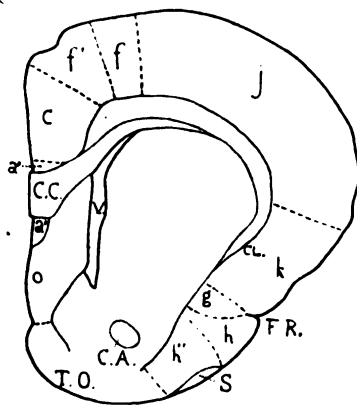


FIG. 21.—*Mus decumanus*. Frontal section of the hemisphere. $7\frac{1}{2}$ mag. Camera lucida drawing.

Area *a''* is not large. Its extent is demonstrated by Fig. 19. As is always the case area *a* is lost in the olfactory tubercle. Between *a* and the place where both hemispheres of the brain are united once more a region *o* free from cortex is existing.

Area *c* is situated above the *a*-areas. It shows all cortical layers as in other rodents. Below a rather narrow layer of supra-granular pyramids is a still narrower layer of pale, inflated or non-inflated granules. Beneath this layer a broad lamina ganglionaris does exist, built up of inflated but rather deeply-stained pyramidal cells. The breadth of this layer diminishes in equal proportions with the whole cortex, but upon an average it is as broad as the layers III and IV together. Below the infra-granular pyramids is a polymorphous layer of inflated cells and other ones, more than half as broad as layer V. Area *c* is indicated in Figs. 19 and 21. It extends in a caudal direction till the middle of the corpus callosum.

In the usual way area *c* borders upon an area *d*, being radiating and agranular. The pyramidal cells of the layers III and V are deeply-stained and non-inflated but small. The layers themselves are nearly completely united, as only very few granules, scattered among the pyramids, indicate a granular layer. The inflated cells of the polymorphous layer are lying undermost. Area *d* is easily distinguished from its neighbour, area *f*. Indeed, it is agranular and radiating, and it has smaller pyramids. This especially comes out in horizontal sections. Only Fig. 19 is showing area *d*.

Passing from the median side of the frontal lobe to the lateral, one meets two areas: f and its radiating form f' . Area f (compare Figs. 18, 19, 20 and 21) tapers backward, as it always does. It is constructed by a rather narrow layer III, only somewhat broader than that layer in area c , but contrarily built up of typical deeply-staining pyramids. Beneath it the very narrow layer IV follows, richer in small deeply-staining pyramids than in non-inflated granules. Layer V, broader than III and IV together, is distinguished by its many deeply-staining pyramids. In the deepest parts of the layer they have been substituted for the greater part by inflated pyramids. The polymorphous layer is very distinctly composed of two layers, separated by a narrow band poor in cells. Immediately below the infra-granular pyramids exists a layer rich in cells, small pyramids as well as inflated cells. Then comes a narrow band poor in cells followed by a band of polymorphous cells about equally broad and contrasting both to the pale-tinted myelum below and the pale-tinted band above.

Area f' much resembles area f , but it is radiating (the infra-granular pyramids are elongated). Moreover, its granular layer is still more vague than in f , and the polymorphous layer is hardly or not divided into two layers by a pale band. It is probable that, wherever there is sufficient curvature of the surface, area f assumes the structure of f' (compare Figs. 19, 20 and 21).

Area k , situated above the claustrum, deviates from the condition observed in the rabbit and the squirrel. At least I am not able to discern an area k in front of an area k' , but I find already granules in the anterior portions of k . I am unable to describe the structure of this area, because it varied much in my serial sections. The homology of the area cannot be doubted as the claustrum is too obvious a means of recognition.

In one of the series of frontal sections area k possessed a layer III of typical non-inflated pyramids above a granular layer, somewhat narrower and indistinct, with deeply-staining, stellate granules. These sometimes assumed the shape of pyramids. Their number was not large, much less than the number of granules in area j . The granular layer was succeeded by layer V, nearly as broad as III and IV together, and consisting of deeply-stained, typical but rather small pyramids. Some inflated cells are scattered among them. Layer VI was narrow and composed of inflated cells and small pyramids. Undermost came the claustrum with its inflated, but very deeply-stained cells.

In the other series of frontal sections, however, and in the series of horizontal sections, the supra-granular pyramids were inflated or they approached to it. The granules were obviously inflated; the inflated cells outweighed in number in layer V, and all non-inflated cells were lacking in layer VI. Only the claustrum agreed with that in the other series.

As some spots of area *k* in the first-mentioned series of frontal sections did too possess inflated cells, I come to the conclusion that inflated and non-inflated pyramids are indeed the same kind of cells. I remarked this already in *Lepus cuniculus*.

Area *k* has been projected in Fig. 18, and it is also visible in Fig. 21.

The claustrum is not exclusively situated below area *k*, but it comes even ventrally of the rhinal fissure, which fact has been stated for other animals by Livini, Röthig and Ernst de Vries (1910). Where this is the case an area *k''* is situated above the claustrum. I did not recognise this area in the rat before I had seen it in *Dipodomys*. One can find its projection in Fig. 18 below the rhinal fissure, and it consists of the layers III, V and VI similarly constructed to those of area *k*, but somewhat narrower, and a granular layer with only very few inflated granules and contrasting as a light band. In one of the series of frontal sections all cells were inflated except the supra-granular pyramids.

More frontally area *g* occupies the bottom of the rhinal fissure. It is visible in Fig. 21, but not in Fig. 18, as its projection is overlapped by the projection of other areas. Its extent agrees with that of area *g* in *Sciurus* to which I can refer. The inflation of the supra-granular pyramids is a characteristic which makes this layer scarcely differ from the granular cells beneath. The layers V and VI are composed of inflated but rather deeply-staining cells. The claustrum is absent underneath this area. As it is occupying the ventral part of the frontal lobe of the hemisphere it borders upon area *d*.

Ventrally of the rhinal fissure there is an area, which I shall call *h + h''*. For in some spots it has the structure of *h*, i.e., a layer of crowded, deeply-staining pyramidal cells above some scattered cells and a polymorphous layer. But somewhere else it shows the structure of *h''*, i.e., a layer of inflated pyramids above some scattered cells and a polymorphous layer. These two types, however, are not separated so as to form two distinct areas, as in the rabbit, but they are irregularly mixed. Only this seems to be the rule, that beneath the olfactory tract only *h''* occurs, as is indicated in Fig. 21. I united both areas in the projection (Fig. 18) to area *h + h''*. They are just visible in Fig. 19, the median projection of the hemisphere.

Area *j* is occupying about the same place as it did in the rabbit and the squirrel. It is obvious by a quality of the granular layer which I will indicate by the word: clouded. As in other rodents the granules of this area, being non-inflated ones in this case, are more numerous and more crowded together than in any other area. Now in this layer spots occur where the tissue between the ganglion cells takes an extraordinarily deep stain. According to Isenschmid

(1911) this must be ascribed to the great local density of the fibrils in this layer.* It contributes a spotted aspect to this layer, already obvious with low power. This is still increased by the upper part of layer V being poor in cells and consequently very pale-tinted. The result is a row of deeply stained spots above a light band. The deep spots are only small, $\frac{1}{8}$ to $\frac{1}{10}$ mm. in diameter. They are separated by extremely narrow strips with the usual light tint of the background. After all I would consider this area *j* to be a dimorphous one, the first type having deeply-stained fibre tissue in the granular layer, the other type without this phenomenon and with less granules. The first type is divided into a great number of extremely small areas, which are surrounded by the second type.

I found a "clouded" area *j* only in the three representatives of the genus *Mus*. So typical a quality renders the homologisation of the areas, which are demonstrating it, to a nearly undisputable fact. Upon one thing I must lay great stress. If the clouds are seen distinctly, then the material must have been preserved in formalin. Some waltzing-mice, the brains of which were not placed into formalin, showed the clouds hardly at all.

As to the other layers of area *j*, there is a layer of deeply-staining supra-granular pyramids about twice as broad as the granular layer, a lamina ganglionaris being a mixture of stout deeply-staining pyramids and inflated cells, which are rather widely dispersed, and a polymorphous layer not differing from that layer in area *f*. The latter is divided into two by a narrow layer poor in cells. Area *j* has been indicated in Figs. 18, 20 and 21.

Between the areas *j* and *f* lies an area which agrees with *n* of *Sciurus* by its situation, but also by the fact that it contains the largest pyramidal cells of the rat. For these reasons I shall call it area *n*. It is visible in Figs. 18, 19 and 20. As to its structure it closely corresponds to area *j*. The layers III and VI have not changed, but layer V is distinguished by its many huge pyramids and its few inflated cells. The granular density of layer IV is generally great but rather unequal. This is the cause of an inequality of tint which recalls the clouds of area *j*, but never reaches their distinctness. The granules of area *n* are non-inflated ones.

Laterally and caudally of area *n* I found an area which I have called *m'*. Partly it occupies the place of an area *u* (compare Fig. 19), and this points, as in *Lepus cuniculus*, to a relation between the areas *u* and *m* or *m'*.

Area *m'* is radiating. The layer of deeply-staining supra-granular pyramids is rather narrow. The granular layer is narrow and poor in cells, but distinctly developed. The layer of infra-granular pyramids is broad, but rather poor in

* Isenschmid seems not to have observed this phenomenon to be especially manifest in this area. Compare also page 344.

cells. In its upper part are pyramids, which are obvious by their large size. Layer VI consists of inflated cells with very small pyramids scattered among them. It is not divided as it is in area *n*. Besides, in Figs. 19 and 20 area *m'* is visible in Fig. 22.

The large temporal area is once more area *p* (Figs. 18, 20 and 22). Its structure is not exactly the same everywhere, but there is no question about a sub-division into more than one area or even about dimorphy. Plate II, Fig. 3, is an illustration of this area. It is very well distinguished from area *j*. Layer III is similar to that of area *j*, but the granular layer is narrow, has only few non-inflated granules and is not clouded. The lamina ganglionaris is nearly separated into two layers; a superior one only consisting of inflated cells, and so having the appearance of a second granular layer, and an inferior one containing besides deeply-staining, typical pyramids. Numerous inflated cells form the polymorphous layer. Close to the myelum I found a narrow

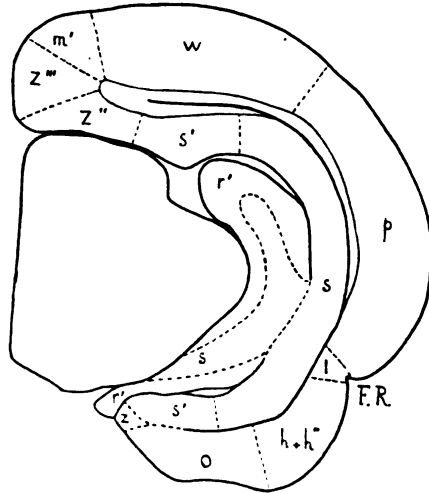


FIG. 22.—*Mus decumanus*. Frontal section of the hemisphere. $7\frac{1}{2}$ mag. Camera lucida drawing.

layer of spindle-shaped cells, but the narrow layer poor in cells of area *j* is lacking. This is an obvious difference.

A small part of the bottom of the rhinal fissure is occupied by an area, which can be homologised with area *l* of *Sciurus*. It does not allow of projection, but it is visible in Fig. 22. It occurs in a hundred sections in the neighbourhood of the one drawn in Fig. 22. Frontally and caudally of this area the areas *p* and *h + h''* border upon one another. Area *l* is characterised by the absence of supra-granular pyramids. The zonal layer is reached by the granular layer, composed of non-inflated granules. The layers V and VI are clearly present, but they are narrow, as area *l* is compactly constructed everywhere.

Area *w* once more is covering the occipital lobe like a cap (Figs. 18, 19, 20 and 22). It has a well-developed layer of typical supra-granular pyramids and a granular layer, which by its distinct development and richness in non-inflated granules offers a ready means of recognising this area. Layer IV is much more distinct and richer in granules than that of area *p*, but it is not particularly broad. Layer V has more true pyramids and less inflated cells

than the corresponding layer in area *p*, but the pyramids are of a small size. Also in the polymorphous layer there are more pyramidal cells, and the number of the inflated cells has been reduced as compared with area *p*. The cellular density of the layers V and VI is greater in area *w* than in *p*.

On the lateral side two areas below the rhinal fissure remained undescribed until now. One of them is area *h'*, but it is both small and indistinct as compared with the corresponding areas in *Sciurus* and the rabbit. As usual, the layer of supra-granular pyramids (which are deeply stained) has a greater breadth than in *h*, and its cells are more or less grouped. The sub-division into two layers, which I found indicated in the rabbit, is manifest in the rat. The superior layer, III^a, is narrow and has large cells, the inferior one, III^b, on the contrary, is broad and composed of smaller cells. A narrow layer poor in cells follows underneath, in its turn followed by a narrow layer with few infra-granular pyramids, which may be indistinct. Undermost is a polymorphous layer with many inflated cells.

Towards the median side *h'* borders upon a region where numerous inflated cells exist, but they are so irregularly situated that I shall consider this region free from cortex (Fig. 19, *o*). I only indicated area *h'* in Fig. 18.

Area *x* is situated caudally or rather dorsally from area *h'*. The light band, immediately observed, proves the homology of this area with the *x*-areas of *Sciurus* and *Lepus cuniculus*, but its structure deviates in some respects. For, above the layer free from cells, which is, moreover, narrow here, there are obviously two cell-layers. The superior one consists of pyramidal cells which may be inflated or not, but which are always deeper of tint than the inflated pyramids of the inferior layer. Moreover, the latter layer is one and a half times as broad. I consider both these layers belong to layer III. The fourth layer free from cells is not followed by infra-granular pyramids, but immediately by the round inflated cells of layer VI. Area *x* has been projected in Figs. 18 and 19.

The fascia dentata (*r'*) is again composed of a layer of crowded, non-inflated granules above some dispersed inflated or stellate cells. The cornu ammonis (*s*) is a layer of inflated pyramids lying closely to one another. Both areas have been projected; as one area *r' + s* in Fig. 19. Area *s* is again accompanied by the well-known transitional area *s'*, where the pyramids are more dispersed, but they are also non-inflated and consequently deeply stained. I could not totally project it, as is demonstrated by Fig. 19. I indicated the areas *r'*, *s* and *s'* too in Fig. 22.

Posterior to the hippocampus a group of areas is situated which agree in situation as well as in structure with some of the *z*-areas in the rabbit. Area *z* (Figs. 19 and 22) is agranular. It consists of a layer of small, typical supra-

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granular pyramids above a layer of inflated and non-inflated infra-granular pyramids and a polymorphous layer of inflated cells. Between the layers III and V, as well as between the layers V and VI, a narrow layer free from cells is indicated, but it is very indistinct.

Area z'' (Figs. 19 and 22) again wants a third layer. So the non-inflated granules reach the zonal layer. They lie above a layer of inflated infra-granular pyramids, about as broad as layer IV. A rather narrow polymorphous layer composed of deeply staining cells is existing undermost.

Area z''' too is present in the rat. It is visible in Figs. 19 and 22, and is composed, firstly, of a narrow layer of crowded, inflated, supra-granular pyramids. Then follows a layer of non-inflated granules twice as broad. Its cells are closer crowded together where they are more near layer III. The lamina ganglionaris is twice as broad as the layers III and IV together. Some deep pyramids are scattered among the inflated cells of which it is constructed. The cells of layer V are widely dispersed. The polymorphous layer is formed by small deep cells, and is about as broad as layer V.

Finally, there is a narrow area between z'' and m' which reminds me of z^{iv} by its situation, but differs too much from it in its structure to be named by this letter. I shall call it aa (Fig. 19). The layers III and IV only deviate from those of area z''' by their being twice as narrow. Beneath them is a broad layer of infra-granular pyramids, all deeply stained and rather elongated. Also in layer VI the cells are more obviously pyramids than in area z''' .

Mus decumanus.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
I	Area a.	
V	Typical pyramids.	
I	Area a'.	Deeply staining.
III	Narrow	Typical pyramids	Cells crowded together.
IV	Inflated granules.	
V	Inflated pyramids.	
VI	= V	Inflated cells.	
			This area has a very compact structure. Layers V and VI may be pushed away in the neighbourhood of the corpus callosum.

Layer.	Breadth.	Cells.	Further Remarks	
<i>Area a".</i>				
I	Similar to VI of <i>a'</i>	
V	$1\frac{1}{2} \times VI$	Inflated pyramids.		
VI		
<i>Area c.</i>				
I	Inflated or non-inflated granules.	
III	Narrow		
IV	Narrower than III	Inflated or non-inflated granules.		
V	Broad, = III + IV	Inflated but rather deep pyramids.		
VI	$\frac{1}{2} \times V$	Inflated cells and other ones.		
<i>Area d.</i>				
I	On the limit of III and V.	
III	Small non - inflated pyramids.		
V	Small non - inflated pyramids		
VI	Inflated cells.		
<i>Area f.</i>				
I	The layer is somewhat broader than III of <i>c</i> .	
III	Narrow	Typical pyramids		
IV	Very narrow....	More deep pyramids than non - inflated granules.		
V	Broader than III + IV.	Deep pyramids; in greater depths inflated pyramids.		
VI	Many cells.	
<i>Area f'.</i>				
I	Composed of two layers separated by a light band. The superior layer has many small pyramids and inflated cells; the inferior layer has polymorphous cells.	
III		
IV		
V		
VI		
<i>Area g.</i>				
I	More vague than in <i>f</i> .	
III		
IV		
V		
VI	Not divided into two layers. This area is radiating. In other respects it is similar to <i>f</i> .	
<i>Area g.</i>				
I		
III	Inflated pyramids		
IV	Inflated granules		
V	Inflated pyramids		
VI	Inflated cells		
I	Cells resembling granules. Not numerous cells.	
III		
IV		
V		
VI	Cells rather deeply staining.	
I		
III		
IV		
V		
VI		

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Layer.	Breadth.		Cells.	Further Remarks.
<i>Areas h + h".</i>				
I
III	Inflated or non-inflated pyramids.	Cells crowded together.
IV	Only a few scattered cells.
VI
<i>Area h'.</i>				
I
IIIa	Narrow	Large deep pyramids.
IIIb	Broad	Small deep pyramids.
IV	Narrow	This layer is poor in cells.
V	Narrow	Pyramids	Few cells ; the layer is indistinct.
VI	Inflated cells	Many cells.
<i>Area j.</i>				
I
III	2 × IV	Deep pyramids.
IV	This layer is clouded.
V	Stout deep pyramids and inflated cells.	Superior part of this layer poor in cells.
VI	Similar to VI of <i>f</i> . This area is dimorphous.
<i>Area k.</i>				
I
III	Non-inflated pyramids.
IV	Narrower than III	Deep stellate granules	Much less granules than in IV of <i>j</i> .
V	= III + IV	Small typical pyramids.
VI	Narrow	Inflated cells and small pyramids.
Clastrum	Deep inflated cells.	Sometimes all cells in III, IV and VI and most of them in V are inflated.
<i>Area k".</i>				
I
III	Narrower than in <i>k</i>	Similar to III of <i>k</i> ; cells never inflated.
IV	Inflated granules	Very few cells ; contrasting as a light band.
V	Narrower than in <i>k</i>	Similar to V of <i>k</i> .
VI	Narrower than in <i>k</i>	Similar to VI of <i>k</i>
Clastrum
<i>Area l.</i>				
I
IV	Non-inflated granules.
V	Narrow
VI	Narrow
				This area is compactly con- structed.

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area m'.</i>			
I
III	Rather narrow	Deep pyramids.	Poor in cells.
IV	Narrow	Rather poor in cells.
V	Broad	Large pyramids in the upper parts.
VI	Inflated cells and very small pyramids.	This area is radiating.
<i>Area n.</i>			
I
III	Similar to III of <i>j</i> .
IV	Non-inflated granules....	Granular density great but unequal.
V	Many huge pyramids and few inflated cells.	The largest pyramids of the rat.
VI	Similar to III of <i>j</i> .
<i>Area p.</i>			
I
III	Similar to III of <i>j</i> .
IV	Narrow	Non-inflated granules....	Few cells.
V	Inflated cells in the superior part.	Typical pyramids underneath.
VI	Inflated cells	Many cells; close to the myelum a narrow layer of spindle-shaped cells.
<i>Area r'.</i>			
I
IV	Narrow	Non-inflated granules....	Cells crowded together. Some scattered inflated or stellate cells beneath IV. This area is fascia dentata.
<i>Area s.</i>			
I
V	Inflated pyramids	Cells crowded together. This area is cornu ammonis.
<i>Area s'.</i>			
I
V	Deep non-inflated pyramids.	Cells more dispersed than in <i>s</i> .
<i>Area w.</i>			
I
III	Typical pyramids.
IV	Non-inflated granules....	Rich in cells, very distinct.
V	Small typical pyramids and inflated cells.	More true pyramids and less inflated cells than in <i>p</i> .
VI	Pyramids and inflated cells.	More pyramids than in <i>p</i> .
			The cellular density of V and VI is greater than in <i>p</i> .

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area x.</i>			
I	
IIIa	Inflated or non-inflated pyramids.	Cells deeper than those of IIIb.
IIIb	$1\frac{1}{2} \times \text{IIIa}$	Inflated pyramids.	
IV	No cells....	Contrasting as a light band.
VI	Round inflated cells.	
<i>Area z.</i>			
I	
III	Small typical pyramids.	
V	Inflated or typical pyramids.	
VI	Inflated cells.	A narrow light band between III and V and between V and VI. This area is agranular.
<i>Area z'.</i>			
I	
IV	Non-inflated granules.	
V	= IV....	Inflated pyramids.	
VI	Narrow	Deeply-staining cells.	
<i>Area z''.</i>			
I	
III	Narrow	Inflated pyramids	Cells crowded together.
IV	$2 \times \text{III}$	Non-inflated granules....	Cells closer crowded together near III.
V	$2 \times \text{III} + \text{IV}$	Inflated cells and some deep pyramids.	Cells widely dispersed.
VI	= V	Small deep cells.	
<i>Area aa.</i>			
I	
III	$\frac{1}{2} \times \text{III of } z''$	Similar to III of z'' .
IV	$\frac{1}{2} \times \text{III of } z'''$	Similar to IV of z''' .
V	Broad	Deep and rather elongated pyramids.	
VI	Cells more obvious pyramids than in z''' .

Mus musculus (L.).

The brain of the mouse, as might be expected, conforms more with that of the rat than with brains of the squirrel or of the rabbit. It is so smooth that even the rhinal fissure does not extend posterior of the frontal end of the olfactory tubercle. Notwithstanding [two shallow fissures have a constant

position, the one caudally of the olfactory tubercle, the other more backward in the temporal region (Fig. 23), none of them may be considered to be the rhinal fissure.

Three serial sections of the mouse were studied, two frontal and one horizontal one. They were all three sections of the whole brain and consequently of both hemispheres.

Two of these mice were wild, the third one was a tame white mouse with black spots. The results agreed sufficiently.

Again beginning with the cortical area, which is pierced by the fore end of the corpus callosum, one observes this to be again area *a'*. It shows the typical deeply staining zonal layer above a narrow layer of crowded supra-granular pyramids. Then follows a fourth layer, nearly free from cells, with but few granules. Below this the layer of infra-granular pyramids is present, as broad as the layers I, III and IV together. Polymorphous cells are lying undermost in an indistinct layer. Area *a'* has been projected in Fig. 24 and is also visible in Fig. 26. It continues its way above the corpus callosum as a narrow band, and is passing downward into the olfactory tubercle. It may be that an area *a*, which would be expected between *a'* and the olfactory tubercle, is present, but the line of demarcation common to it and to the cortex of the tuberculum could hardly be indicated. So it does not occur in my projection.

Area *a''* occupies more space in the mouse than it did in the rat. It consists of a broad layer of inflated, infra-granular pyramids above a somewhat narrower layer of polymorphous cells, stained more deeply than the pyramids. In one of my series the infra-granular pyramids were perfectly round and, moreover, surrounded by a clear space, such as to resemble inflated granules in a high degree. By this fact area *a''* recalled area *b* of *Sciurus*. It differs, however, from this by the absence of layer V. Without any doubt, therefore, the mouse has an area *a''* and not an area *b*. Area *a''* has been indicated in Fig. 24.

Area *c* (Figs. 24 and 26) is present in its usual place above the areas *a'* and *a''*. It possesses all cortical layers, *i.e.*, firstly, a zonal layer above a very narrow layer of inflated supra-granular pyramids. This layer contains only some rows of cells, and it is followed by a broad layer of inflated granules. Then comes a layer of infra-granular pyramids about equally broad and containing deep, non-inflated or light, inflated cells. Finally, there is a polymorphous layer of inflated and non-inflated pyramids. The breadth of the area as a whole varies considerably (compare Fig. 26). Generally speaking, the cells of this area have a paler tint than those of the neighbouring area *f'*.

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Area *d* again appears where it might be expected (Fig. 24). It is agranular and radiating. The polymorphous cells can be distinguished from the united infra- and supra-granular pyramids by their more rounded shape and their somewhat paler tint. Area *d* differs from *f'* by its smaller infra-granular pyramids and because any indication of a granular layer is wanting.

Area *f'* (Fig. 24, 25 and 26) is radiating like *d*. The zonal layer is obviously

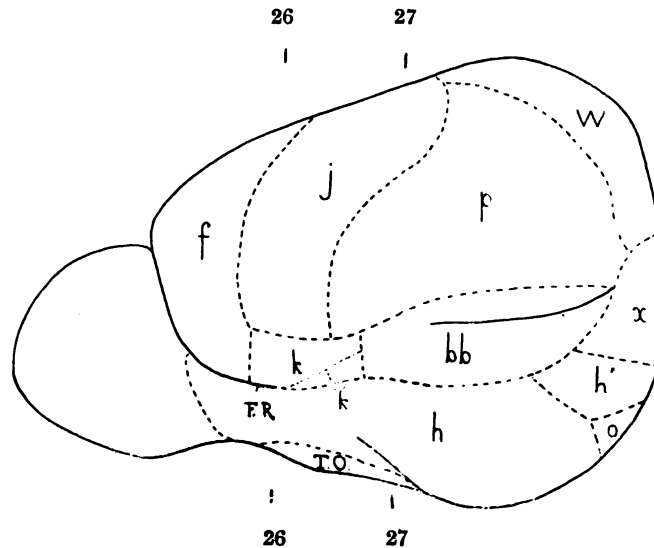


FIG. 23.—*Mus musculus*. Lateral projection of the hemisphere. 10 mag. The cyphers 26 and 27 indicate the level of the sections represented by Figs. 26 and 27.

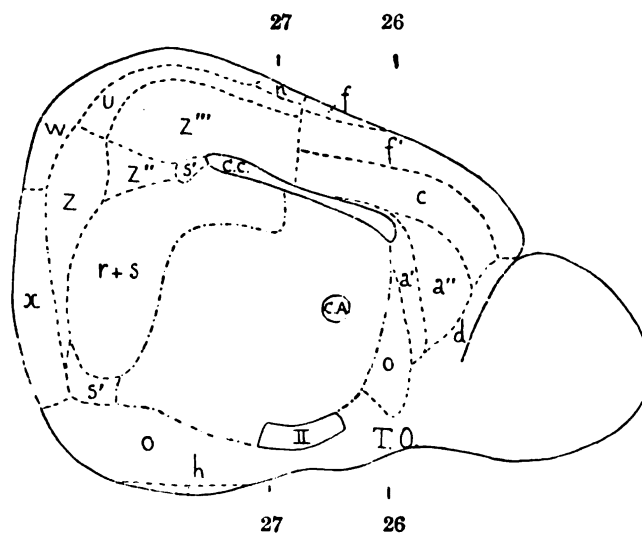


FIG. 24.—*Mus musculus*. Median projection of the hemisphere. 10 mag.

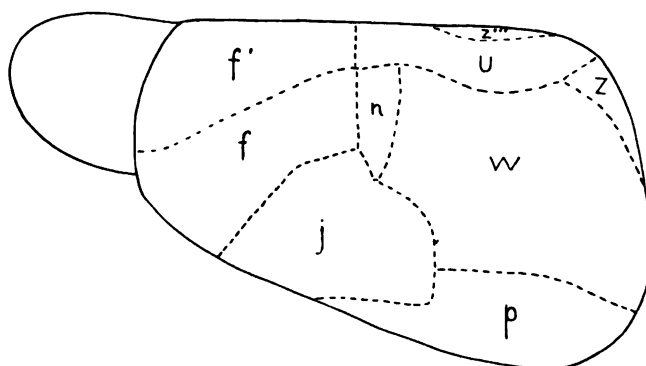


FIG. 25.—*Mus musculus*. Dorsal projection of the hemisphere. 10 mag.

narrower than that of area *c*. Below this is a distinct layer of typical, deep supra-granular pyramids. It is followed by a fourth layer, which contains no granules, but only some small pyramids. One recognises layer IV to be a layer by its poverty in cells, and so although this layer is present, it is permissible to call *f'* an agranular area. Layer IV is followed by a broad lamina ganglionaris with rather large and very deep pyramidal cells. It is situated above a polymorphous layer, half as broad and composed of deep cells of various shapes.

The difference between *f* and *f'* is caused by the fact that layer III is one and a half times broader in *f* than in *f'*. Moreover, there is a granular layer above it, narrower than layer III. It consists of non-inflated granules, which are widely dispersed, when compared with those of area *j*. The fifth layer is broad and contains stout, deep pyramids. Layer VI, about equally broad as V, is again constructed of deeply staining, polymorphous cells. A division into two layers, as I observed in the rat, is indicated in the mouse. But this limit is too indistinct to be a means by which the area can be recognised. The shape of area *f* principally agrees with that of the rodents described already (compare Figs. 23, 24, 25 and 26).

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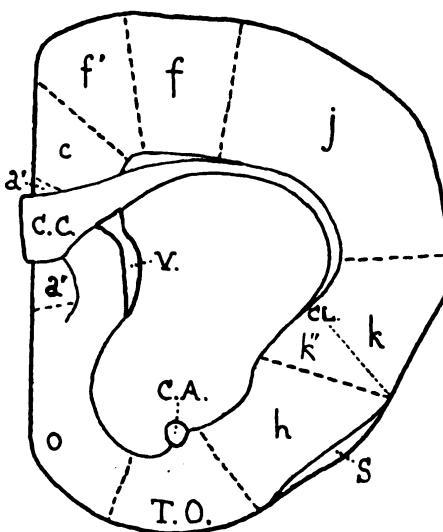


FIG. 26.—*Mus musculus*. Frontal section of the hemisphere. 15 mag. Camera lucida drawing.

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The ventral side of the frontal lobe of the hemisphere is occupied by area *g*. It is not visible in any one of the figures, but to get an idea of its situation I may once more refer to *Sciurus*. Area *g* is extending backward till *k* is reached. It only consists of inflated cells, nowhere forming distinct layers, consequently the structure of this area is still more indistinct than in the other rodents.

Frontally the rhinal fissure forms the dorsal limit of area *h*. Its supra-granular pyramids are deep and non-inflated everywhere, and thus an area *h''* is not present. For the rest area *h* has the characters previously described. It extends far backward and runs dorsally of the olfactory tubercle (Fig. 23). It is present in the sections represented by Figs. 26 and 27.

Caudally of *f*, I find area *j*, which can be homologised with *j* in the rat, because its granular layer shows the same peculiar clouds. I shall not give another description of them here. The layer of supra-granular pyramids, generally of a deep tint, is well developed. The granular layer is nearly equally

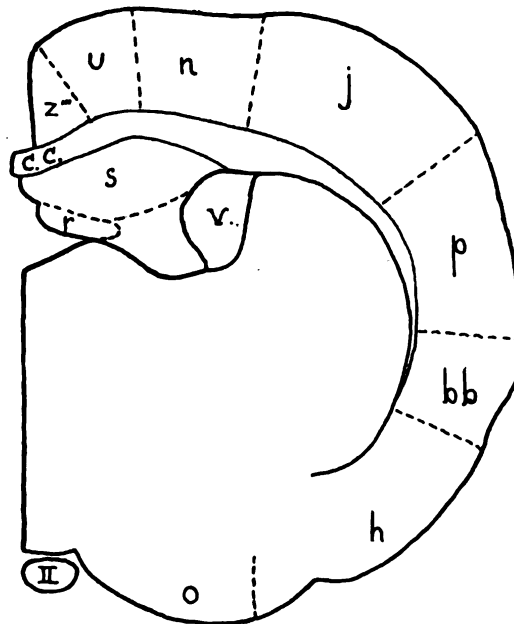


FIG. 27.—*Mus musculus*. Frontal section of the hemisphere.
15 mag. Camera lucida drawing.

broad. Its non-inflated granules are very much crowded together. The superior portion of layer V, characterised by few inflated cells, is broader proportionally than in the rat. This is the cause of a very distinct light band beneath the clouds. In the inferior part of the lamina ganglionaris are well developed, deeply staining pyramids.

The polymorphous layer, as broad as IV and V together, is composed of deep cells of various shapes. Compare for area *j* Figs. 23, 24, 26 and 27.

The claustrum, which in the mouse is comparatively small, lies, as in the rat, below two areas, *k* and *k'*. Area *k* is the more important of them. One can find it ventrally of area *j* in its usual place (Figs. 23 and 26). It consists of a narrow layer of supra-granular pyramids being inflated in one series and non-inflated in another one. The granular layer which then follows is broad, but poor in cells. It is situated above the layers V and VI, both about equally broad. The polymorphous layer, however, is composed of paler cells than layer V, and they have no true pyramidal shape.* The claustrum with its deep, round or spindle-shaped cells lies undermost.

I did not recognise the rather small area *k'* in the mouse before I had seen the corresponding area in *Dipodomys*. But now I am sure of its presence, as, moreover, I could recognise it in the rat and as I. de Vries (1911) seems to indicate the same area by the frontal part of his area L. Area *k'* is situated ventrally of area *k*. Only its caudal portion could be projected (Fig. 23), as its frontal part is overlapped by other areas. As the rhinal fissure is not manifest, one cannot exactly say whether area *k'* extends ventrally of it, as it did in the rat, but probably its position is quite the same. In structure it chiefly differs from area *k* by the want of cells in layer IV, which consequently contrasts as a light band. Moreover, all other layers are narrower than in area *k*. Area *k'* is not present in the mouse.

Posterior to the areas *f* and *j* is a small area *n*, characterised, like *n* in the rat, by giant pyramids. At least, the narrow layer V contains very many infra-granular pyramids of a much larger size than those of other areas. Layer III does not differ from that of area *j*. The granular layer is rich in non-inflated granules, but it is not quite as broad as in *j*, and it shows no clouds. The polymorphous layer is as broad as III and IV together. It contains large cells, especially in the neighbourhood of the myelum. Area *n* is visible in Fig. 27 and its projection in Figs. 24 and 25.

I observed the temporal area *p* to be situated caudally of area *j*. In the mouse it has very few characteristic features. Yet the lines of demarcation with the surrounding areas are distinct as their structure is quite typical; in the last degree this is the case with area *w*. No dimorphy could be detected. The lamina pyramidalis of area *p* does not differ from that of the areas *j* or *w*. The granular layer is about as broad as layer III, but it shows no clouds and has less granules than in *j*. Layer V contains neither particularly many, nor particularly large pyramidal cells. There are less of them in this area than in area *j*, and certainly less than in area *w*. The polymorphous layer is not different from that of *j*. I indicated area *p* in Figs. 23, 25 and 27, and made a drawing of its structure (Plate II, Figs. 4 and 8).

* I cannot grant the absence of layer V to Ernst de Vries (1910).

Ventrally of *p* one finds an area, which by its structure somewhat resembles area *l*, but on account of its extent I cannot homologise it with *l*. As I could not detect its homologon in the rat, I shall name it with a new letter, *bb*. Area *bb* (compare for its situation Figs. 23 and 27) is an agranular one. The layer of supra-granular pyramids is broad, broader than in area *p*. The granular layer is totally wanting, and layer V may only be distinguished from III by its pyramidal cells being larger. Inflated pyramids never occur in this area. A layer of deep, polymorphous cells, about as broad as the layers III or V, is present below layer V. Area *bb* is the continuation of the areas *k* and *k'*, but one cannot confound them, because the claustrum is not under *bb*. Without any doubt, the development of this area is connected with the absence of a rhinal fissure in these regions.

As in other rodents, area *w* is occupying the occipital lobe like a cap (compare Figs. 23, 24 and 25). Layer V is still the most characteristic layer of this area. The deeply staining pyramids in it are crowded together, and they are of a very short type. The granular layer is narrow, but the deep granules are numerous. Layer III is broad, but its pyramids to a certain degree resemble granules, as they are so short. In consequence of this, the limit between the layers III and IV can hardly be detected. The polymorphous layer has no peculiarities. The cortex as a whole is markedly thinner than in the areas *j* or *p*. I estimate the cortical thickness in area *w*, as only $\frac{3}{4}$ or $\frac{2}{3}$ of that in the areas *j* or *p*.

Area *h* is passing backward into area *h'*. In the mouse the cells are here so irregularly scattered that the area has the appearance of a region free from cortex. Yet, whoever had seen the area in *Sciurus* or the rabbit would be able to recognise it in the mouse too. The layer of supra-granular pyramids, which are deeply staining, is broad, and the cells in it are grouped. It lies above a layer poor in cells, and under this follows a layer of deep polymorphous cells. Area *h'* can hardly be recognised in frontal sections on account of its situation, but it is very easily seen in horizontal sections. Area *h'* has been projected in Fig. 23.

Area *x* joins the latter area. In *Mus musculus*, too, it does not appear as distinctly as possible. Yet its situation and structure sufficiently agree with those of the *x* area in other rodents to homologise it with them. The pale-tinted band, poor in cells, is not pronounced because it is narrow. The supra-granular pyramids above it are separated into two distinct layers, III^a and III^b. The superior one, III^a, is narrow; its cells are very deep, and they are similarly grouped as they are in *h'*. The inferior layer of supra-granular pyramids, III^b, is twice as broad as the superior one; its cells are not so deep, and they are not grouped. I observed under the layer poor in cells only a

layer of deep polymorphous cells, about as broad as layer III^b. Area x is especially clear in horizontal sections. It has been projected in Figs. 23 and 24.

It is easy to recognise the fascia dentata and the cornu ammonis. I indicated them in Fig. 27, and I projected them together as $r + s$ in Fig. 24. The granules of the fascia dentata without doubt are inflated. For this reason I shall name the area, as in *Sciurus*, with r and not with r' , as I did in *Mus decumanus*. Some stellate cells are scattered in the usual way beneath the granules of area r . Area s is nothing but a layer of inflated pyramids much crowded together. The usual area s' , a transition into the neighbouring areas, is present. The pyramids in it become more and more dispersed. The projection of s' is only partly visible (compare Fig. 24).

Posterior to the hippocampal formation a group of z -areas exists which completely agrees with that group in the rat. In area z (projected in Figs. 24 and 25) all granules are absent. It shows a broad layer of rather deep pyramids, probably being the united layers III and V, as I would judge from area z in *Lepus cuniculus*. But I could not detect any difference between III and V, and so it is possible that layer III or layer V is totally absent, and only layer V or layer III remains. Below the pyramidal layer one observes a pale band, poor in cells. It is much broader in the mouse than in the rabbit. The light band is about four times narrower than the pyramidal layer. Undermost is a polymorphous layer, with deep cells, about three times as broad as the light band.

If I had not had occasion to compare the structure of this area with its structure in other rodents, then I certainly would have taken the light band for layer IV, and in consequence thereof the pyramidal layer for layer III. By means of comparative anatomy, however, I got the preceding opinion.

Area z'' , projected in Fig. 24, can be immediately homologised with area z'' of the rat, because the supra-granular pyramids are wanting. In consequence of this, the non-inflated granules, forming a broad layer, are reaching the zonal layer. Below them a narrow layer of not numerous and small infra-granular pyramids follows, and then a polymorphous layer, equally broad, but with somewhat paler and larger cells than those of layer V.

Area z''' occupies about the same place as it did in the rat (Fig. 24). It also agrees with it in its structure. The small supra-granular pyramids are crowded together in a very narrow layer. In the granular layer underneath, the non-inflated granules, as they are nearer layer III, are more crowded together. Layer V is broad, but its cells are dispersed. Besides large, deep pyramids also paler tinted cells occur. Layer VI, narrower than layer V, is composed of deeply staining polymorphous cells. Area z''' has been indicated also in Figs. 27 and 25.

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The last area, which has to be described, agrees with area *u* of the rat. I have drawn it in Figs. 24, 25 and 27. The area is agranular and radiating. It is more or less the continuation of *f'*, but differs from it by its large infra-granular pyramids, approaching in size those of area *n*. The layer of deep supra-granular pyramids is rather broad. It is separated from the lamina ganglionaris by a narrow strip, where the cells are more dispersed. Granules are totally absent. The infra-granular pyramids, although rather varying in size, are generally larger than the supra-granular ones. Layer V gradually passes into layer VI. It, too, consists of small deeply staining pyramids.

I found in the mouse more differences in the appearance of the cortical areas in different individuals than in the other described rodents. Yet, I am convinced that other investigators will be able to recognise the areas by the place they occupy, if possibly they may be unable to recognise them by my description of their structure.

Mus musculus.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area a'.</i>			
I		Pyramids	Deeply staining.
III	Narrow	Granules	Cells crowded together.
IV			Few cells.
V	= I + III + IV		
VI		Polymorphous cells	Indistinct layer.
<i>Area a''.</i>			
I		Inflated pyramids	Sometimes these cells resemble granules.
V	Broad		
VI	Narrower than V	Polymorphous cells	Cells staining deeper than infra-granular pyramids.
<i>Area c.</i>			
I		Inflated pyramids	Only a few rows of cells compose this layer.
III	Very narrow		
IV	Broad	Inflated granules.	
V	= IV	Deep, typical or light and inflated pyramids.	
VI		Inflated and non-inflated pyramids.	
			The cells of this area are paler than those of area <i>f'</i> .

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area d.</i>			
I	The pyramids of III and V are not well distinguished. Cells more round and paler than those of V. This area is agranular and radiating.
III	
V	
VI	
<i>Area f.</i>			
I	Similar to III of <i>f'</i> . Cells widely dispersed.
III	$1\frac{1}{2} \times$ III of <i>f'</i>	
IV	Narrower than III	Non-inflated granules...	
V	Broad	Stout deep pyramids.	
VI	= V	Deep polymorphous cells.	A division into two layers is indicated.
<i>Area f'.</i>			
I	Narrower than in c	Only a few cells.
III	Typical deep pyramids.	
IV	Small pyramids	
V	Broad	Large and very deep pyramids.	
VI	= $\frac{1}{2} \times$ V	Deep cells of various shapes.	This area is radiating.
<i>Area g.</i>			
I	No distinct layers.
III + IV + V + VI	Inflated cells	
<i>Area h.</i>			
I	Cells crowded together. Only a few scattered cells
III	Deep non-inflated pyramids.	
IV	
VI	
<i>Area h'.</i>			
I	Cells grouped. This layer is poor in cells. The cells are very irregularly scattered in this area.
III	Broad	Deep pyramids	
IV	
VI	Deep polymorphous cells.	
<i>Area j.</i>			
I	This layer shows "clouds." Many deep pyramids near VI.
III	Deep pyramids.	
IV	= III	Non-inflated granules...	
V	Few inflated cells near layer IV.	
VI	= IV + V	Deep cells of various shapes.	

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Layer.	Breadth.	Cells.	Further Remarks.
Area k.			
I			
III	Narrow	Inflated or non-inflated pyramids.	
IV	Broad		Poor in cells.
V	= VI		
VI			Cells paler than in V and no true pyramids.
Clastrum		Deep, round or spindle-shaped cells.	
Area k''.			
I			
III	Narrower than in area k.		No cells in this layer.
IV			No cells in this layer.
V			
VI			
Clastrum			Similar to area k in other respects.
Area n.			
I			
III			
IV	Narrower than IV of j.	Many non-inflated granules.	Similar to III of j.
V		Many very large pyramids.	These pyramids are the largest ones of the mouse.
VI	= III + IV	Large cells.	
Area p.			
I			
III			
IV	= III		Similar to III of j or w.
V		Pyramids of moderate size.	Less granules than in area j.
VI			Less pyramids than in w.
Area r.			
I			
IV	Narrow	Inflated granules	Cells crowded together.
			Some scattered stellate cells beneath IV. This area is fascia dentata.
Area s.			
I			
V		Inflated pyramids	Cells crowded together.
			This area is cornu ammonis.
Area s'.			
I			
V			Cells more dispersed, but similar to V of area s.
Area u.			
I			
III	Rather broad	Deep pyramids.	
V		Large pyramids	Larger pyramids than in f'.
VI		Small deep pyramids.	III and V are separated by a narrow band where the pyramids are more dispersed. This area is agranular and radiating.

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area w.</i>			
I			
III	Broad	Very short pyramids	Pyramids often resembling granules.
IV	Narrow	Numerous deep granules	
V		Deep, very short pyramids.	Pyramids crowded together.
VI		Polymorphous cells.	
			The whole cortex is thinner in this area than in <i>j</i> or <i>p</i> .
<i>Area x.</i>			
I			
IIIa	Narrow	Deep pyramids	Pyramids grouped.
IIIb	= 2 × IIIa	Pyramids	Cells paler than in IIIa and not grouped.
IV	Narrow		Poor in cells, this layer is a light band.
VI	= IIIb	Polymorphous cells.	
<i>Area z.</i>			
I			
III + V	Very broad	Deep pyramids.	
Light band	$\frac{1}{2} \times III + V$		Poor in cells, broader than in the rabbit.
VI ...	3 × light band	Deep polymorphous cells.	
			This area is agranular.
<i>Area z''.</i>			
I			
IV	Broad	Non-inflated granules.	
V	Narrow	Few small pyramids.	
VI	= V	Paler and larger cells than in V.	
<i>Area z'''.</i>			
I			
III	Very narrow....	Small pyramids	Cells crowded together.
IV		Non-inflated granules.	Cells crowded together near layer III.
V		Large deep pyramids	Pale tinted cells between the pyramids.
VI	Narrower than V	Deep polymorphous cells.	
<i>Area bb.</i>			
I			
III	Broad		This layer is broader than in <i>p</i> .
V	= III	Larger pyramids than those of III.	
VI	= III	Deep polymorphous cells.	
			This area is agranular. Its pyramids are never inflated ones.

Mus Wagneri var. rotans (Japanese Waltzing-Mouse).

It was impossible to me to distinguish the brain of the Japanese waltzing-mouse by its outer appearance from that of *Mus musculus*. I could not even observe it to be smaller, although *Mus Wagneri var. rotans* is smaller than *Mus musculus* indeed (compare Droogleever Fortuyn, 1912). This is corroborated by the fact that the skulls, too, of both animals are indistinguishable.

I cut the brain of seven individuals of *Mus Wagneri var. rotans*, six in a frontal direction, and one in a horizontal one. It would be too boldly speaking if I pretended not to have found any mutual differences between these serial sections, or to have observed no differences when comparing them with my three serial sections of *Mus musculus*. But the maps published of the house-mouse can remain unaltered as to the waltzing-mouse, and there is not one striking difference in the cortical structure which holds good in all series (compare in regard to area *p* the chapter on the auditory cortex).

So I can generally refer to *Mus musculus* in regard to the description of the cortical areas in the waltzing-mouse. I only wish to remark, that the five series of brains, which I received from Dr. Quix, were generally showing inflated pyramids in areas, where both other series of animals from "Artis" and also those of *Mus musculus* had typical, deep pyramids. In consequence thereof the cortical structure in these series was much more indistinct, because the limits of layers and areas had become vague. I do ascribe this to the different preservation. Certainly, Dr. Quix has preserved the brains in a fresher state than I was able to do, and so his way of preservation cannot be called worse than mine. But I placed the brains into formalin for some time, and to this or to some other difference I ascribe the different results.

In four cases the brains cut by me were of full-grown animals; one waltzing-mouse was two and two other waltzing-mice were three months old when they were killed, and their brains were preserved. They do not give rise to any remarks. They were not even smaller than full-grown brains.

Of two series of frontal sections and one series of horizontal sections only every second section was stained with methyleneblue. The other sections were stained with Heidenhain's hæmatoxylin. In this way I obtained some series which certainly will keep their colour, but they did offer nothing new.

Lepus europaeus (Pall.).

The brain of the hare in general resembles that of the rabbit in a high degree. Yet it is more troublesome to study it, as the differences between

many areas have been greatly reduced. Especially the areas *f*, *j*, *p* and *w* are less differentiated than in other rodents.

As in the rabbit a rhinal fissure and a fissura sagittalis lateralis (Figs. 28, 29 and 30) are present.

I studied two serial sections of *Lepus europaeus*, a frontal and a horizontal one, each through a hemisphere of the same individual.

Let the first section to be described be again a section through the frontal end of the corpus callosum (Fig. 31). As in the rabbit, here I observe above the corpus callosum a small area, exclusively consisting of a layer of pyramids. It is the well-known area *a*. As usually it proceeds towards the olfactory tubercle (Fig. 29).

Above area *a* the areas *c* and *c'* occupy a corresponding situation to that in the rabbit (Fig. 31). Both areas are showing the layers I, III, IV, V and VI. The supra- and infra-granular pyramids are non-inflated and deeply staining. In *c* most granules are non-inflated, and they somewhat resemble pyramids from which they can be distinguished by their rounder shape and paler tint. The granular layer is more indistinct in *c'* than in *c*; the granules are not so numerous there. Besides area *c'* differs from *c* by the peculiar stripes, which also area *c'* in the rabbit is showing. There is less difference between *c* and *c'* in the hare than in the rabbit. I do not think that the extent of *c'* is quite similar to that in the rabbit. Area *c'* is not proceeding as far backward as *c* does (Fig. 29). Both areas are just visible in Fig. 30.

Area *d* is not very typical in the hare. It differs from the neighbouring area *f* by its being quite agranular and radiating. Layer III is narrow and distinguished from V by its somewhat smaller pyramids. The difference between the layers V and VI, too, is only indicated by the smaller size of the pyramids in VI. Area *d* is visible in Fig. 29.

Area *f'* (Fig. 31) is radiating. A rather narrow layer of deep supra-granular pyramids is followed by a very narrow granular layer, half as broad as layer III, and with deep granules. The lamina ganglionaris below it is broad, and its pyramidal cells are large and elongated. This layer is nearly one and a half times as broad as III and IV together. Layer VI, as broad as layer V, differs from it by smaller pyramidal cells and its possessing polymorphous cells in its inferior parts.

Area *f'* does not extend so far frontally as it usually does (Figs. 28, 29 and 30).

The layers III and IV of area *f* are both similarly constructed to those of *f'*, but they are nearly twice as broad. Layer IV has inflated granules at the side of non-inflated ones. The ganglionic layer is characterised by many large infra-granular pyramids, being the largest ones, which the hare

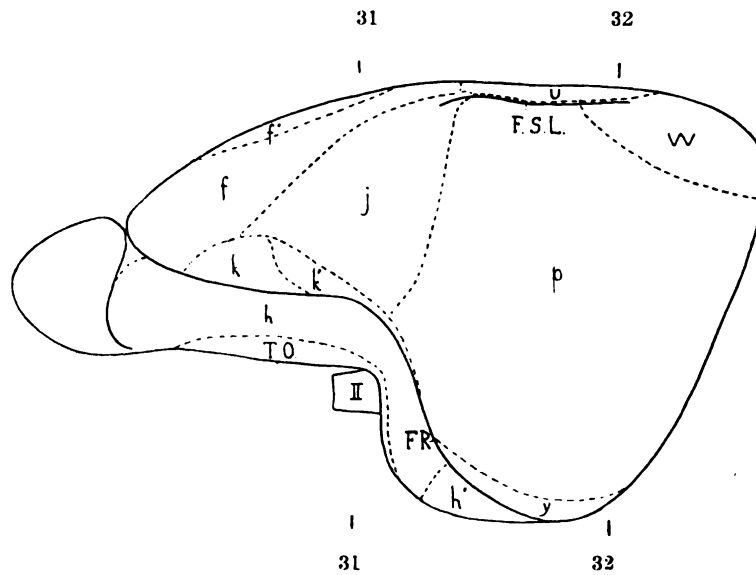


FIG. 28.—*Lepus europaeus*. Lateral projection of the hemisphere. 3 mag. The cyphers 31 and 32 indicate the level of the sections represented by Figs. 31 and 32.

is demonstrating. The layer is narrower than layer V in *f'*. A polymorphous layer, as broad as IV and V together, and composed of round or polygonal

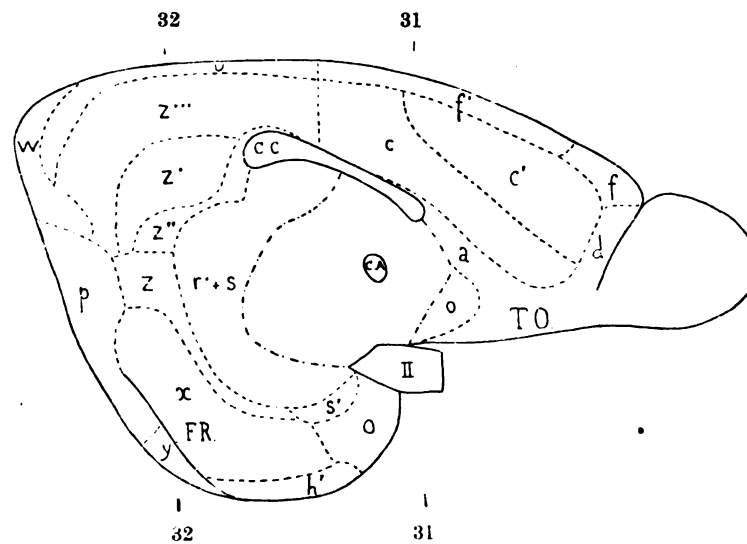
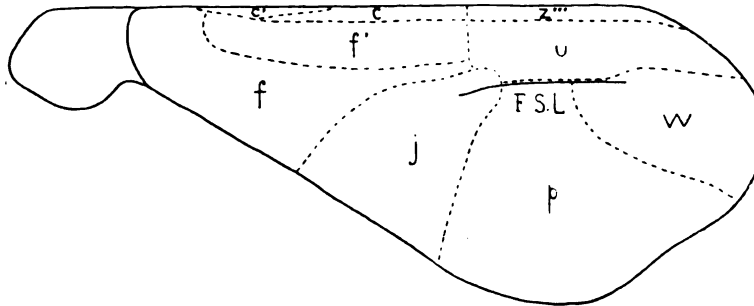


FIG. 29.—*Lepus europaeus*. Median projection of the hemisphere. 3 mag.

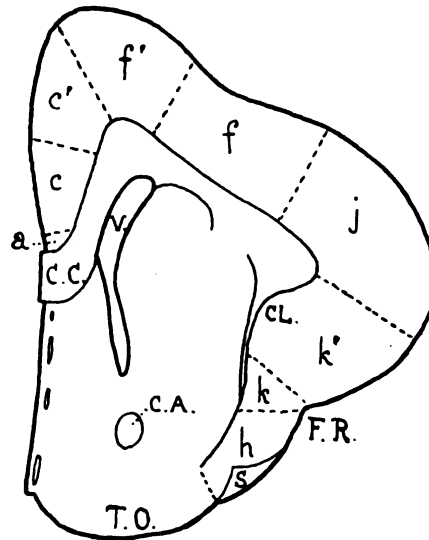
FIG. 30.—*Lepus europaeus*. Dorsal projection of the hemisphere. 3 mag.

cells, follows undermost. The projection of *f* is visible in Figs. 28, 29 and 30. Area *f* occupies its usual place.

Area *g* is poorly developed in *Lepus europaeus*. It commences to occupy the bottom of the rhinal fissure about on the same level where *k* has reached its utmost breadth (compare Fig. 28).

From that point it proceeds frontally and becomes broader, but it only occupies a rather small portion of the ventral side of the frontal lobe. This latter is chiefly occupied by the areas *f* and *d*. The structure of area *g* is rather indistinct. There is no claustrum under it, which forms a point of difference from area *k*. The layers are all narrow. The supra- and infra-granular pyramids are small and scarcely pyramidal-shaped so as to resemble much the cells of layer VI. The granular layer is particularly poor in cells and very narrow.

The region lying above the claustrum consists once more of the areas *k* and *k'*. The former is distinguished by its few granules. The shape of the hemisphere renders the areas less projectable than they were in other rodents. I indicated them in Figs. 31 and 28. Area *k* consists of a narrow layer of small supra-granular pyramids. It is followed by a layer poor in cells, but not free from them. A few deep granules are scattered in it. The layer of

FIG. 31.—*Lepus europaeus*. Frontal section of the hemisphere. 6 mag. Camera lucida drawing.

infra-granular pyramids is about as broad as III and IV together, but it is indistinct, because the pyramids are small and rather pale-tinted. The polymorphous layer is composed of still paler cells of various shapes. The claustrum is built up of deeper cells, variously shaped. Area *k'* chiefly, if not only, differs from *k*, because there are pretty many granules, inflated and deep ones, in layer IV.

The only area in the frontal half of the hemisphere ventrally of the rhinal fissure and dorsally of the olfactory tubercle is area *h*. It has the well-known structure, *i.e.*, a layer of deeply-staining, crowded pyramidal cells, with some dispersed cells under it. But a polymorphous layer is scarcely or not present. Area *h* is visible in Figs. 28 and 31.

Caudally of *f* one observes area *j*. The multitude of granules, which distinguished it in other rodents, is not obvious in this animal. More granules indeed are present than in area *f*, but I doubt whether there are more than in *p*. A new kind of granules, found in *j* and the neighbouring area *p*, is interesting. They are a kind of giant granules, large, deep granules, much larger than the common non-inflated granules. They are scattered among the inflated and non-inflated granules. I have deliberated whether they might be perhaps "lost" pyramidal cells, as I had often found, but their shape gives them no claim to this name. I did not observe giant granules in the rabbit. On the contrary, I here sometimes found a pyramidal cell between the granules. In the drawing of area *p* of the hare (Plate II, Fig. 5) one can see some giant granules in layer IV.

Layer V offers the principal points of difference from the areas *f* and *p*. The infra-granular pyramids are smaller than they are in *f*, but they are larger than in *p* and sometimes they are less numerous. The layers III and VI afford no peculiarities. The former consists of typical pyramids, the latter of deep cells of various shapes. Area *j* is visible in Figs. 28, 30 and 31.

Area *p* has again a large extent (compare Figs. 28, 29, 30 and 31). I cannot pretend that its structure is very uniform everywhere. Especially the breadth, the number of cells and the distinctness of the granular layer are greatly varying. Yet, I could not distinguish two types, and therefore I should not like to call this area a dimorphous one. Layer IV has less inflated granules than in area *j*. Here and there giant granules do occur. Often the granules have been replaced by very small pyramids, this being also the case in area *j*. The lamina ganglionaris has smaller pyramids than in *j*. Except these differences area *p* is similarly constructed to *j*. Consequently, its limits are rather indistinct and this is corroborated by the fact that the differences from area *w* (compare later on) are also very slight. As to the structure of this area compare Plate II, Fig. 5.

Where area *k* has come to an end the bottom of the rhinal fissure is occupied by an area *l*. It extends till near the section, represented by Fig. 32, as it is ending just in front of it. Its projection is overlapped by those of other areas, and so it is not indicated in any one of the figures. Its structure is rather indistinct, and if I had not seen in other rodents a more distinct area *l*, I probably would not have found it in the hare. It is compactly constructed

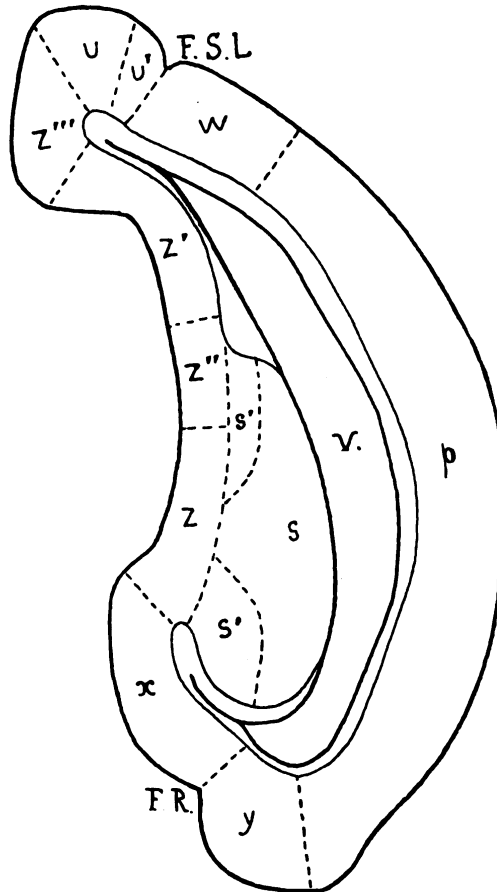


FIG. 32.—*Lepus europaeus*. Frontal section of the hemisphere.
6 mag. Camera lucida drawing.

and consists of a rather broad layer of small supra-granular pyramids. The fourth layer is nearly free from cells. Layer V is only built up of some deep pyramids, and below this is a rather broad polymorphous layer being poor in cells.

Area *y* (Figs. 28, 29 and 32) is of more importance. It is radiating and nearly agranular. Between the supra- and infra-granular pyramids some

granules are present. They compose a narrow and indistinct lamina granularis interna. The infra-granular pyramids are elongated, and especially layer V differs from that layer of area *p*, because it is composed of small, elongated pyramids. Area *y* shows in some degree the stripes of area *c'*.

Backward, below the rhinal fissure, area *h* passes into area *h'*. Here the layer of supra-granular pyramids is broader than in *h*, and its cells are grouped, as I observed in all other rodents. Below the lamina pyramidalis some scattered pyramids are present. They do not form a true layer, but a kind of transition into layer III^b of the neighbouring area *x*. Below these pyramids is a layer poor in cells, and then follows a layer of pale-tinted polymorphous cells. Area *h'* is visible in Figs. 28 and 29.

Area *x* has a more distinct structure in the hare than in the other rodents which have been described already. Layer III^a is twice or three times narrower than layer III^b, and it has obviously larger pyramidal cells. The light band, poor in cells (layer IV), is obvious and has about the breadth of layer III^a. Below this layer IV in the first place a layer of deep infra-granular pyramids is following and then a polymorphous layer of smaller, rounder and paler cells. Both layers are about equally broad and as broad as layer III^a. Area *x* has been indicated in Figs. 28, 29 and 32.

A portion of area *o*, which is free from cortex and situated frontally of area *x* (Fig. 29), has its cells in some degree arranged into layers. Yet, I could not consider it a different area, as, moreover, it does not occur in other rodents.

Area *w* of the hare is small as well as it is very indistinct. Its limit with area *p* can hardly be indicated. Its most obvious character is the poverty in cells of layer V. The pyramids in it are widely dispersed, although they are well developed. Only few cells of other shapes are lying among them. In my opinion the granular layer is somewhat smaller than in area *p*, but in other respects it does not differ greatly. The lamina pyramidalis is not different from that of area *p*. In layer VI the cells are less numerous. The inferior parts of layer V show the greatest poverty in cells. So, an obvious light band is present between the layers V and VI. Area *w* has been drawn in Figs. 28, 29, 30 and 32.

Mesially area *w* borders upon area *u*, which reaches the fissura sagittalis lateralis. In this case too sufficient reasons were wanting to consider the bottom of this fissure a different area. Area *u* is more or less radiating because the infra-granular pyramids are elongated, and because also layer VI consists of small but proportionally long pyramids. Both layers are about equally broad, and especially layer V may be called well developed. The granular layer is very narrow and built up of very small, deep granules. Layer III, although narrow, is well developed and rich in stout supra-granular pyramids.

As in the rabbit, a portion of this area deviates somewhat in its structure. In a narrow band the pyramids of the layers V and VI are still more elongated than in the other parts of area *u*. This band borders upon the fissura sagittalis lateralis. Even in Fig. 30 it would be hardly projectable, but I indicated its limits in Fig. 32. In this band the supra- and infra-granular pyramids are also more numerous, and the granules are less numerous than in the typical area *u*.

If I call this portion *u'*, then *u'* ends where the fissura sagittalis lateralis becomes shallow. As in rodents without this fissure no homologon of this area can be found, I should like to consider it no more than a transitional region.

Area *u*, including area *u'*, is visible in Figs. 28, 29, 30 and 32.

Once more, the hippocampal formation consists of two areas. The cornu ammonis (*s*) is a layer of pyramids closely crowded together; the fascia dentata, *r'*, is a layer of non-inflated granules, above some scattered, stellate cells. As always, the areas *r'* and *s* have been projected together in Fig. 29. Moreover, area *s* is visible in Fig. 32, in a place where it cannot be projected. As might be expected, a transitional area *s'* is present. Here the pyramidal cells are more widely dispersed. Besides in Fig. 32, I indicated its projection in Fig. 29.

The group of *z*-areas of the rabbit was also found in the hare, except area *z''*, the place of which has been totally occupied by *z'''*. He who is acquainted with the areas in *Lepus cuniculus*, will immediately recognise them by their structure in *Lepus europaeus*, although the position occupied by them is somewhat different.

Area *z'''* (Figs. 29, 30 and 32) has a narrow but distinct layer of supra-granular pyramids. Below this is a layer of small granules about one and a half times as broad. Then layer V follows about as broad as III and IV together, and characterised by large and widely dispersed pyramids, with few cells of other shapes between them. Layer VI is narrow, half as broad as V; it is composed of small, deep cells, partly of pyramidal shape. Here and there large pyramidal cells have deviated into the layers III or IV. This also happens to be the case in the areas *z'* and *z''*.

Area *z''* (Figs. 29 and 32) is similarly constructed to area *z'''*, but the supra-granular pyramids are absent. So the granular layer joins the zonal layer. In some places it can be even as broad as layer V. In contradistinction to area *z'* of the rabbit it proceeds frontally above the corpus callosum to a certain extent. The highly curved form of this area renders its projection (Fig. 29) greatly distorted.

Area *z'* chiefly differs from *z'''* by its layer of supra-granular pyramids being twice as narrow and its granular layer being twice as broad. The area is visible in Figs. 29 and 32.

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Finally, area *z* is once more an agranular area. Below a broad layer of small supra-granular pyramids is a layer of larger subgranular pyramids, about twice as narrow. Underneath is a polymorphous layer as broad as layer V, and separated from it by a very narrow layer poor in cells. Area *z* has been indicated in Figs. 29 and 32.

Lepus europaeus.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area a.</i>			
I	
V	Pyramids.	
<i>Area c.</i>			
I	
III	Narrow	Non-inflated, deep pyramids.	
IV	Broader than III	Non-inflated granules.	
V	= VI....	Non - inflated, deep pyramids.	
V	
<i>Area c'.</i>			
I	
III	Narrow	Similar to III of <i>c</i> .
IV	Broader than III	Less granules than in <i>c</i>	This layer is less distinct than in <i>c</i> .
V	Narrower than VI	Similar to V of <i>c</i> .
VI	Similar to VI of <i>c</i> .
			This area shows the peculiar stripes of area <i>c'</i> in the rabbit.
<i>Area d.</i>			
I	
III	Narrow	Smaller pyramids than in V.	
V	Pyramids.	
VI	Smaller pyramids than in V.	
			This area is radiating and agranular.
<i>Area f.</i>			
I	
III	$1\frac{1}{2} \times$ III of <i>f'</i>	Similar to III of <i>f'</i> .
IV	$1\frac{1}{2} \times$ IV of <i>f'</i>	Inflated and non-inflated granules	
V	Narrower than V of <i>f'</i>	Many large pyramids....	These pyramids are the largest ones of the hare.
VI	= V + IV	Round or polygonal cel's.	

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area f'.</i>			
I	
III	Rather narrow	Deep pyramids.	
IV	$= \frac{1}{2} \times \text{III}$	Deep, non-inflated granules.	
V	$1\frac{1}{2} \times \text{III} + \text{IV}$	Large elongated pyramids	
VI	$= \text{V}$	Small pyramids and polymorphous cells.	This area is radiating.
<i>Area g.</i>			
I	
III	Narrow	Small pyramids	Pyramids sometimes similar to polymorphous cells.
IV	Very narrow	Poor in cells.
V	Narrow	Small pyramids.	
VI	Narrow	Polymorphous cells.	The structure of this area is indistinct.
<i>Area h.</i>			
I	
III	Deep pyramids	Pyramids crowded together.
IV	Some scattered cells in this layer.
VI	Very indistinct.
<i>Area h'.</i>			
I	
III	Broader than III of <i>h</i>	Pyramids	Cells grouped, some scattered pyramids below them.
IV	Poor in cells.
VI	Pale, polymorphous cells.	
<i>Area j.</i>			
I	
III	Typical pyramids.	
IV	Inflated, non-inflated and giant granules.	Granules not particularly numerous.
V	Pyramids smaller than in <i>f</i> but larger than in <i>p</i> .	
VI	Deep cells of various shapes.	
<i>Area k.</i>			
I	
II	Narrow	Small pyramids.	Poor in cells.
IV	Deep granules	This layer is indistinct.
V	$= \text{III} + \text{IV}$	Small, pale pyramids	
VI	Pale polymorphous cells.	
Clastrum	Deep cells of various shapes.	

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Layer.	Breadth.	Cells.	Further Remarks.
Area <i>k'</i> .			
I	Rather many granules.
III	
IV	Inflated and deep granules.	
V	
VI	
Clastrum.....	
In other respects similar to <i>k</i> .			
Area <i>l</i> .			
I	Nearly free from cells.
III	Rather broad	Small pyramids.	
IV	
V	Few deep pyramids.	
VI	Rather broad	
Poor in cells.			
Area <i>p</i> .			
I	Less granules than in <i>j</i> ; variable structure. Smaller pyramids than in <i>j</i> .
III	Typical pyramids.	
IV	Inflated and giant granules.	
V	Pyramids	
VI	Deep cells of various shapes.	
.....			
Area <i>r'</i> .			
I	Granules crowded together. Some scattered stellate cells below the granules. This area is fascia dentata.
IV	Non-inflated granules.....	
.....			
Area <i>s</i> .			
I	This area is cornu ammonis.
V	Pyramids crowded together.	
.....			
Area <i>s'</i> .			
I	Pyramids more dispersed than in V of area <i>s</i> .
V	
.....			
Area <i>u</i> .			
I	Rich in cells.
III	Narrow	Stout pyramids	
IV	Very narrow	Very small, deep granules.	
V	Broad	Elongated pyramids.	
VI	= V	Small but relatively long pyramids.	
.....			
This area is more or less radiating. A portion of it, <i>u'</i> , has more numerous and more elongated pyramids and less granules.			

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area w.</i>			
I	
III	Similar to III of <i>p</i> .
IV	Narrower than in <i>p</i>	In other respects similar to IV of <i>p</i> .
V	Large pyramids	Very few cells.
VI	Less cells than in VI of <i>p</i> .
			Between V and VI is a light band, because the inferior parts of V are very poor in cells.
<i>Area x.</i>			
I	
III ^a	Larger pyramids than in III ^b .	
III ^b	2 or 3 × III ^a	Pyramids.	
IV	= III ^a	Granules	Poor in cells; light band.
V	= III ^a	Deep pyramids.	
VI	= III ^a	Small, pale, round cells.	
<i>Area y.</i>			
I	
III	Pyramids.	
IV	Narrow	Few granules	Indistinct layer.
V	Elongated pyramids.	
VI	Small elongated pyramids.	
			This area is radiating and is endowed with the stripes of area <i>c'</i> .
<i>Area z.</i>			
I	
III	Broad	Small pyramids.	
V	$\frac{1}{2} \times$ III	Large pyramids.	
VI	= V	Separated from V by a very narrow layer, poor in cells.
<i>Area z'.</i>			
I	
III	$\frac{1}{2} \times$ III of <i>z'''</i>	
IV	2 × IV of <i>z'''</i>	
V	
VI	
			In other respects similar to <i>z'''</i> .
<i>Area z''.</i>			
I	
IV	About = V	
V	
VI	
			In other respects similar to <i>z'''</i> .
<i>Area z'''.</i>			
I	
III	Narrow	Pyramids	Distinct layer.
IV	$1\frac{1}{2} \times$ III	Small granules.	
V	= III + IV	Large, widely dispersed pyramids and other cells.	
VI	$\frac{1}{2} \times$ V	Small deep cells, sometimes pyramidal-shaped.	
			Some large pyramids have deviated into the layers III and IV.

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Cavia cobaya (Marcgr.).

The hair of the guinea-pig is endowed, besides with a distinct rhinal fissure (Fig. 33, F.R.), with a fissura sagittalis lateralis (Figs. 33 and 35), and a fissura

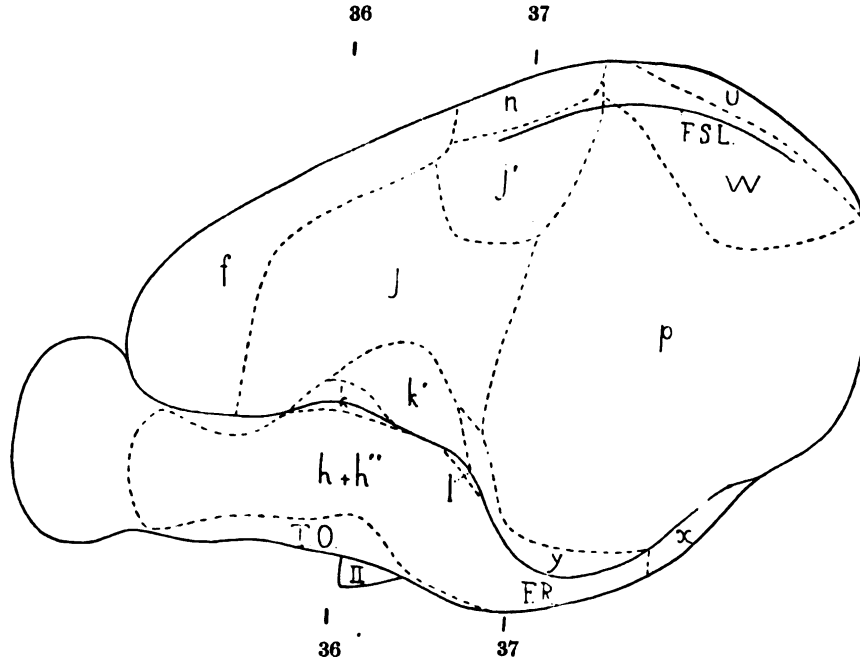


FIG. 33.—*Cavia cobaya*. Lateral projection of the hemisphere. 6 mag. The cyphers 36 and 37 indicate the level of the sections, represented by Figs. 36 and 37.

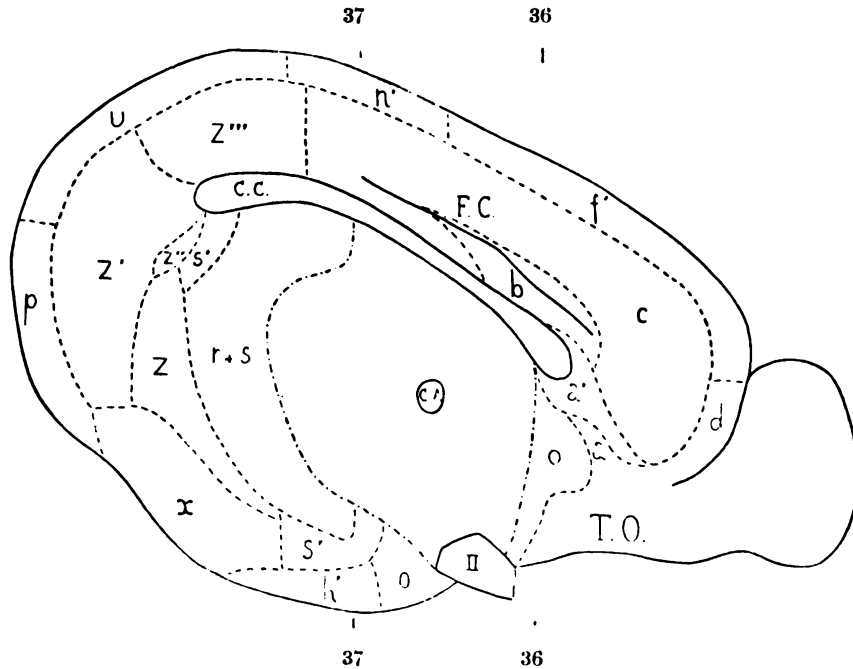


FIG. 34.—*Cavia cobaya*. Median projection of the hemisphere. 6 mag.

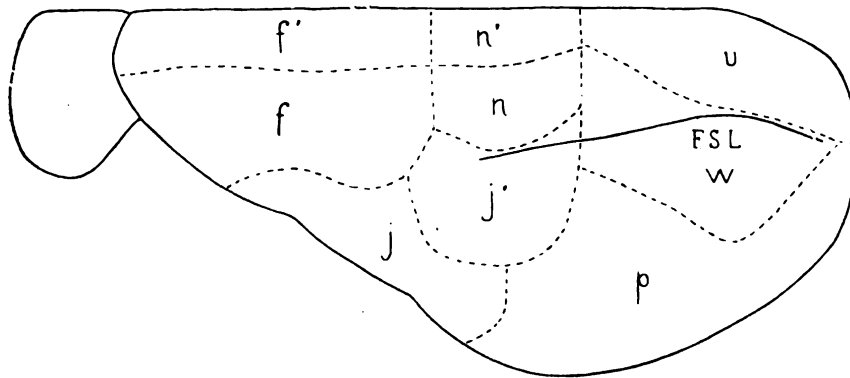


FIG. 35.—*Cavia cobaya*. Dorsal projection of the hemisphere. 6 mag.

cinguli (Fig. 34, F.C.). The latter is here more constant than in the rabbit, and as it can help me in indicating the situation of area *b* I have drawn it in this case. I wish to point out the extraordinary length of the corpus callosum. Three series of *Cavia cobaya* were studied, among which one series of frontal sections of the left hemisphere of one individual. Of both other series of sections through the right and left hemispheres of a second individual, the first was cut parallelly to the hinder border of the occipital lobe, while the other one was cut perpendicularly to it. With this I intended to cut the limits of Brodmann's areas 20, 21 and 22 in such a way as to render them as easily distinguishable as possible. Later on one will learn that even in this way it was impossible to me to distinguish any difference between the areas 20, 21 and 22 of Brodmann, as well as I did not succeed in this in other rodents.

The structure of many areas of the series of frontal sections considerably deviated from that of both other series. This was only in consequence of the pyramidal cells being inflated or non-inflated. I cannot indicate the cause of this phenomenon, as was remarked in the rabbit. The series of frontal sections possessed in many areas inflated pyramids, where they were not present at all in both other series. I shall remark this once more in the description of the cortical areas. Some areas could be more easily recognised in one series, other areas in both other series. But after sufficient investigations the extent of all areas appeared to be the same everywhere. So I may publish without a single objection one set of brain-maps.

As Fig. 36 demonstrates, the frontal end of the corpus callosum is piercing an area, which has to be called *a'*. Its structure is extremely obscure, but in favourable spots the layers I, III, IV, V and VI can be recognised. The area wants these layers to become duly homologised with area *a'* of the genus *Mus*. Besides the zonal layer showed the typical, deep blue stain in the series

of frontal sections, at least near the corpus callosum. All layers are very narrow, especially layer IV, where few granules are present. The supra- and infra-granular pyramids are deeper than the polymorphous cells. The area has been projected in Fig. 34. It is extending far in a frontal direction.

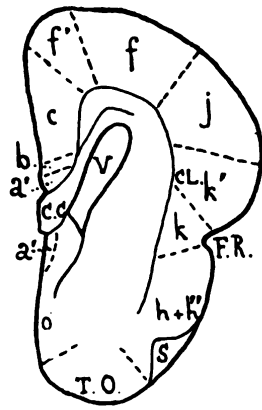


FIG. 36.—*Cavia cobaya*. Frontal section of the hemisphere. 6 mag. Camera lucida drawing.

Ventrally of *a'* area *a* is situated. As usual it consists of a layer of deep pyramids and extends towards the olfactory tubercle.

The guinea-pig has an area which agrees in its structure with area *b* of *Sciurus*. The supra-granular pyramids are totally absent, and the broad layer of inflated granules, as broad as *V* and *VI* together, borders upon the lamina zonalis. The ganglionic layer is narrow and contains few pyramidal cells. If these happen to be inflated, then layer *V* can be scarcely distinguished from layer *VI* with its inflated cells. Area *b* has not at all so large an extent as it had in *Sciurus*. Frontally it surrounds the fissura cinguli (Fig. 34), caudally it only occupies its bottom. Area *b* is also visible in Fig. 36.

I found area *c* in its usual place (Figs. 34 and 36). It is endowed with a layer of supra-granular pyramids, which can be either inflated or not. Below this layer is a broad granular layer with inflated granules. Then follows a layer of infra-granular pyramids, somewhat broader than layer *III*, and composed of generally inflated pyramids. The polymorphous layer is as broad as layer *V* and consists of deep but inflated cells. In the series of frontal sections the area showed the peculiar stripes of area *c'* of the rabbit. This was not the case in both other series, as here the fibre-tissue had not been stained at all. So area *c* of *Cavia* resembles in its structure more *c'* than *c* of the squirrel.

Area *d* again is present in its well-known place (Fig. 34). It is composed of a not very broad layer of deep, supra-granular pyramids, above a layer of deep, non-inflated granules about equally broad. Below this follows a layer of deep, radiating infra-granular pyramids, and undermost is a broad sixth layer, with rather deep polymorphous cells.

Area *f'* has a distinct limit with area *c*, because it never has inflated pyramids. A narrow but obvious layer of supra-granular pyramids is followed by a layer of inflated granules about equally broad. Below this lies layer *V*, radiating, and as broad as *III* and *IV* together. Besides stout, deep pyramids, inflated cells occur in it. This was the case in the series of frontal sections.

In both other series only large or small, but typical pyramids, were present in this layer. Here, too, many granules were deep and non-inflated. Layer VI, broader than V, consists of inflated or at least pale-tinted cells. Area *f'* occupies in the well-known way the dorsal border of the hemisphere (Figs. 34, 35 and 36).

Area *f'* differs relatively little from area *f*. The latter is not radiating, and according to this the layers III and IV are about twice as broad as in *f'*, but the layers V and VI are somewhat narrower. Layer III has in *f* a common breadth, the breadth which it has also in *j*, for instance. The granular layer is very well developed compared with other rodents. It is especially obvious when the granules are inflated ones. Layer V is broad, one and a half times as broad as in area *j*, and it contains stout, typical pyramids. Besides these, inflated cells may occur, which, however, can also have the shape of deep pyramids. Layer VI, broader than V, consists of inflated and pale-tinted cells. Area *f* too occupies its usual place (compare Figs. 33, 35 and 36).

Area *g* commences to occupy the bottom of the rhinal fissure, where area *k* is ending. More frontally it occupies the ventral side of the frontal lobe. As its projection would be overlapped by that of other areas, I have not projected it, and so it is not visible in any one of the figures. To obtain a better idea of its situation, I refer once more to the squirrel. The area generally shows deeply staining supra-granular pyramids, which are more or less grouped. These cells, however, can be inflated too. The layers IV and V are about as broad as the lamina pyramidalis. The granular layer contains few inflated granules. The pyramids of layer V can be typical and deeply stained or they can be inflated. In this case the layer is indistinct. About layer VI not much can be remarked; its cells are inflated.

Area *j* (Figs. 33, 35, 36 and 37) has a broader granular layer than *f*, and more granules than either this area or area *p*. The layers III and V are both narrower than the corresponding layers of area *f*, and the large pyramids in

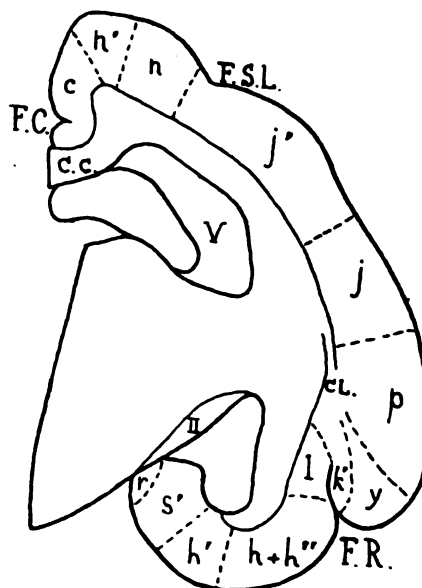


FIG. 37.—*Cavia cobaya*. Frontal section of the hemisphere. 6 mag. Camera lucida drawing.

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V are less numerous. The polymorphous layer does not differ from that of area *f*. The granules of layer IV and most of the cells of V and VI can be either inflated or not.

Very interesting is an area, situated caudally and dorsally of *j*, which was only visible to me in the series of frontal sections with inflated cells and pale-tinted fibre-tissue. It differs in its granular layer from *j*, and this layer shows in some degree the clouds of area *j* in the genus *Mus*. Moreover, remarkably many and remarkably large pyramidal cells were scattered among the granules of layer IV. As these are the only differences from area *j*, and as the clouds are a phenomenon formerly attributed to area *j*, I will call this area *j'*. Indicated by this letter one will observe it in Figs. 33, 35 and 37.

Ventrally of area *j* are the areas *k* and *k'* with the claustrum beneath them. They are nearly similarly constructed, but area *k* has obviously less granules in layer IV than *k'*. The claustrum is considerably narrower below area *k*, and as a whole *k* is compactly constructed on account of the neighbourhood of the rhinal fissure. The areas *k* and *k'* possess a well-developed layer of supra-granular pyramids, which can be inflated.

In *k'* this lies above a granular layer with many granules. In area *k* this layer is twice as narrow and poorer in cells; yet it is not obvious as a light band by its poverty in cells. The layer of infra-granular pyramids, which can be nearly all inflated, is much broader in *k'* than in *k*. The same can be said about layer VI. The claustrum consists of deeply-staining, more or less spindle-shaped cells.

Area *k* is visible in Figs. 33 and 36. It extends some distance ventrally of the rhinal fissure. Area *k'* has been indicated in Figs. 33 and 36, and the section represented by Fig. 37 is one of the most caudal ones which contain this area.

Ventrally of the rhinal fissure an area is situated which possessed inflated pyramids between non-inflated ones in the series of frontal sections (but not in both other series). As these inflated pyramids do not form a different area, but, as they are more or less irregularly scattered among the other ones, I shall call this area *h + h''*, as I did in the rat. It is visible in Figs. 33, 36 and 37.

Caudally of area *k'* a narrow area is situated. It never descends ventrally of the rhinal fissure, but accompanies it to the end. It is radiating and has large infra-granular pyramids. I have to call this area *y*, as in *Lepus cuniculus*. The layer of supra-granular pyramids is narrow and its cells are never inflated. The granular layer is very narrow, still narrower than III. The layer of infra-granular pyramids is broad, and the cells are radiating and elongated.

The polymorphous layer is about as broad as III, IV and V together. It has no structural peculiarities. Area *y* is visible in Figs. 33 and 37.

The bottom of the rhinal fissure from the end of area *k* till its caudal end is occupied by a rather unimportant area *l* with a compact structure. The inflated granules in it lie immediately below the zonal layer, because layer III is absent. Below the granular layer are a poorly developed layer of infra-granular pyramids and a polymorphous layer; together they are somewhat broader than layer IV. The infra-granular pyramids can be inflated or not. Area *l* has been projected in one place (Fig. 33), and has also been indicated in Fig. 37.

Dorsally of area *j'* and caudally of the areas *f* and *f'* two areas are situated only differing from one another because one of them is radiating and the other one not. As here the largest pyramids are present which the guinea-pig possesses, I will call the areas *n* and *n'*. Compared with *Sciurus* their situation more agrees with the areas *m* and *m'*, but their structure not at all. I suppose that the development of area *j'* has shifted area *n* more medially.

Generally speaking, area *n* in its structure more agrees with *j* than with *f*. The layer of supra-granular pyramids, which are never inflated, is well developed, but narrower than in *f*. The granular layer with inflated granules is broader than in *f*; layer V on the other hand is narrower again. But the latter is very obvious by its large, gigantic pyramids. Layer VI has no peculiar characters.

Area *n'* differs from *n* only because it is radiating. The breadth of the layers III and IV has been twice reduced. Layer V is broad and its cells are elongated, and the same can be said about layer VI.

Area *n* is visible in Figs. 33 and 37, *n'* in Figs. 34, 35 and 37.

Area *n'* passes in a caudal direction into an area *u*, which is also radiating. Layer III has about the breadth of this layer in *n'*, and so it is broader than in the neighbouring area *z''*. The cells of this layer are always typical, deep pyramids. The granular layer is somewhat narrower than layer III, and its granules can be either inflated or not. Layer V is characteristic of this area. It contains many stout infra-granular pyramids, but they are smaller than the giant pyramids of area *n'*. Layer V is about as broad as III and IV together. The polymorphous layer is the broadest one. Its cells are staining palely, but the layer shows no other characteristics. Area *u* has been projected in Figs. 33, 34 and 35. Although a *fissura sagittalis lateralis* be present, a region *u'*, as found in the genus *Lepus*, cannot be discriminated.

Laterally of area *u* one observes again area *w*. In the guinea-pig it can rather difficultly be distinguished from area *p*. The granular layer forms

a point of difference because it contains more granules than in *p* and because these granules are obviously larger as they lie more near layer V. Layer III too is somewhat deviating in my opinion. It is as broad as layer IV, but it is more obvious and more regularly built than in area *p*. The supra-granular pyramids are never inflated. The layers V and VI do not differ from those of *p*, at least not from that type of *p*, which possesses non-inflated pyramids. Area *w* has been projected in Figs. 33 and 35.

A large portion of the hemisphere is once more occupied by area *p* (Figs. 33, 34, 35 and 37). The way in which it presented itself in the series of frontal sections was quite a different one from that in which it appeared in both other series. Both forms could scarcely be recognised as the same area. In the series of frontal sections the area was dimorphous and greatly resembled the rabbit in its dimorphy (compare Plate II, Fig. 6). One of both types exclusively consisted of inflated cells, except some "deviated" pyramids in layer IV. Consequently the layers, especially layer V and the polymorphous layer, could hardly be distinguished.* The granular layer had the palest cells of all, and so contrasted with the layers V and III. This type showed sometimes the stripes of area *c*. The other type had a clearer structure. Here all cells of layer III and a great number of those of V were deeply-staining pyramids. The granular layer and layer VI kept their inflated pale-tinted cells. Both types were fantastically mixed, but more or less united by transitions.

In both other series no dimorphy of area *p* could be detected. It resembled *in toto* the second type, as described above. Only the typical pyramids in the layers V and VI were more numerous.

Compared with the areas *j* and *w*, area *p* has always less granules. In many other respects it is rather much agreeing with them. The breadth of the layers was rather variable in this so extensive area.

As area *p* in *Cavia*, for unknown causes, sometimes could conceal its dimorphy, this may be also the case with other areas which I described to be dimorphous areas. This at least holds good for those areas whose dimorphy depends upon the being inflated or typical of the pyramidal cells. I am obliged to lay great stress upon this. Nevertheless, the existence of the dimorphy and its appearance in definite areas (not in all) remain remarkable facts.

Area *h'* is poorly developed. It has the well-known structure, which I shall not describe again, as I can refer to the other rodents. The structure is not very obvious, however. Area *h'* is visible in Figs. 34 and 37.

* Better, however, than in my drawing, Plate II, Fig. 6, to the right, because here no difference in tint of the cells could be indicated. The limits of the cortical layers have been indicated in this figure as I observed them in the section; in the drawing they are nearly invisible.

Area *x* (Figs. 33, 34 and 37) is better developed. I described it already so often that it will be sufficient to say that the layers III^a and III^b can be distinguished. No infra-granular pyramids but only a polymorphous layer occurs below the band free from cells, which represents layer IV.

The cornu ammonis and the fascia dentata too are well-known areas, which can be sufficiently described by a few words. The fascia dentata consists of granules, for the greater part inflated ones. So, it receives letter *r* (Figs. 34 and 37). The cornu ammonis (*s*) is built up of inflated pyramids. One finds this area projected together with *r* in Fig. 34.

The transitional area *s'* was endowed with inflated pyramids in the series of frontal sections, but in both other series with deep, non-inflated pyramids. It has been indicated in Fig. 37 and also in Fig. 34, as far as its projection could be drawn.

Posterior to the hippocampal formation finally a group of *z*-areas is present (areas *z*, *z'*, *z''* and *z'''*), which deviate somewhat by their situation but very little by their structure from the *z*-areas of other rodents. Their situation is demonstrated by Fig. 34. When studying this figure one must mind the difficulties delivered by the projection of the surface of the brain, which is here so peculiarly curved.

As to their structure, I refer to the description given of these areas in other rodents. I will only summarise their most striking points of difference, viz., area *z* is agranular, area *z''* lacks a layer of supra-granular pyramids, this layer is very narrow in *z'*, twice or three times as narrow as the granular layer; in *z'''* the layer of supra-granular pyramids is about as broad as the granular layer.

Cavia cobaya.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area a.</i>			
I	
V	Deep pyramids.	
<i>Area a'.</i>			
I	Staining deeply.
III	Narrow	Deep pyramids.	
IV	Very narrow	Few granules.	
V	Narrow	Deep pyramids.	
VI	Narrow	Polymorphous cells	
			Cells poorer than the pyramids of V.

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Layer.	Breadth.	Cells.	Further Remarks.
Area b.			
I			
IV	= V + VI		
V	Narrow	Few pyramids	Pyramids sometimes inflated.
VI		Inflated cells.	
Area c.			
I			
III		Inflated or typical pyramids.	
IV	Broad	Inflated granules.	
V	Broader than III	Inflated pyramids.	
VI	= V	Inflated, but rather deep cells.	Sometimes this area shows the peculiar stripes of c' in the rabbit.
Area d.			
I			
III	Rather narrow	Deep pyramids.	
IV	= III	Deep, non-inflated granules.	
V		Deep pyramids.	
VI	Broad	Rather deep polymorphous cells.	This area is radiating.
Area f.			
I			
III	2 × III of f'		
IV	2 × IV of f'	Inflated or non-inflated granules.	Comparatively well developed.
V	Narrower than V of f'.	Stout typical pyramids.	
VI	Narrower than VI of f'.	Inflated and pale cells.	
Area f'.			
I			
III	Narrow	Typical pyramids.	
IV	= III	Inflated granules	Sometimes non-inflated granules.
V	= III + IV	Stout, deep pyramids and inflated cells.	
VI	Broader than V	Pale-tinted cells.	
Area g.			
I			
III		Deep pyramids	Pyramids more or less grouped, sometimes inflated.
IV	= III	Few inflated granules.	
V	= III	Inflated or typical pyramids.	Indistinct when the pyramids are inflated.
VI		Inflated cells.	

Layer.	Breadth.	Cells.	Further Remarks.
I		<i>Areas h + h''.</i>	
III		Inflated and non-inflated pyramids mixed.	
IV		Few cells.	
VI			In other respects similar to <i>h</i> of other rodents.
I		<i>Area h'.</i>	
III		Typical pyramids	Cells grouped.
IV	Broad	Few inflated cells.	
VI	Narrow	Pale polymorphous cells.	
I		<i>Area j.</i>	
III	Narrower than in <i>f</i>	Inflated or non-inflated pyramids.	
IV	Broader than in <i>f</i>	Inflated or non-inflated granules.	More granules than in <i>p</i> or <i>f</i> .
V	Narrower than in <i>f</i>	Inflated or non-inflated pyramids.	Less large pyramids than in <i>f</i> .
VI			Similar to VI of <i>f</i> .
I		<i>Area j'.</i>	
III			
IV		Granules and remarkably many pyramids.	This layer is "clouded."
V			
VI			
I		<i>Area k.</i>	
III	Broad	Pyramids, sometimes inflated.	
IV	$= \frac{1}{2} \times \text{IV of } k'$	Few granules.	
V	Narrower than in <i>k'</i>	Typical or inflated pyramids.	
VI	Narrower than in <i>k'</i>	Pale cells.	
Clastrum	Narrower than in <i>k'</i>	Deep, spindle-shaped cells.	
I		<i>Area k'.</i>	
III			
IV		More granules than in <i>k</i> .	
V			
VI			
Clastrum			
			In other respects similar to <i>k</i> , but all layers are broader.

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Layer.	Breadth.	Cells.	Further Remarks.
Area l.			
I	
IV	Somewhat narrower than V + VI.	
V	Inflated or non-inflated pyramids.	Poorly developed.
VI	
Area n.			
I	
III	Narrower than in f	Typical pyramids	This layer is well developed.
IV	Broader than in f	Inflated granules.	
V	Narrower than in f	Giant pyramids and smaller ones.	
VI	
Area n'.			
I	
III	$\frac{1}{2} \times$ III of n	
IV	$\frac{1}{2} \times$ III of n	
V	Broad	Elongated pyramids.	
VI	Broad	Elongated pyramids.	This area is radiating. In other respects it is similar to n.
Area p.			
I	
III	Deep or inflated pyramids.	
IV	Inflated granules and lost pyramids.	Less granules than in j or w.
V	Deep or inflated pyramids.	
VI	Inflated cells.	This area is dimorphous. The breadth of all layers is variable.
Layer r.			
I	
IV	Narrow	Inflated granules	Cells crowded together. Some scattered cells below the granules. This area is fascia dentata.
Layer s.			
I	
V	Narrow	Inflated pyramids	Cells crowded together. This area is cornu ammonis.
Layer s'.			
I	
V	Inflated pyramids or deep pyramids.	Pyramids more dispersed than in s.
Area u.			
I	
III	= III of n'	Typical, deep pyramids.	
IV	Narrower than III	Inflated or non-inflated granules.	
V	= III + IV	Many stout pyramids.	
VI	Broadest layer	Pale cells.	This area is radiating.

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area w.</i>			
I			
III	= IV....	Typical pyramids	More obvious than in <i>p</i> .
IV		Inflated granules	More granular than in <i>p</i> ; larger granules near layer V.
V		Typical pyramids.	
VI			Similar to VI of <i>p</i> .
<i>Area x.</i>			
I			
III ^a		Deep pyramids.	
III ^b	= 2 × III ^a	Inflated pyramids.	
IV			This layer is free from cells and contrasts as a light band.
VI		Pale polymorphous cells.	
<i>Area y.</i>			
I			
III	Narrow	Typical pyramids.	
IV	Very narrow....		
V	Broad	Large pyramids	Cells elongated.
VI	= III + IV + V		This area is radiating.
<i>Area z.</i>			
I			
III	Very narrow....	Very small, deep pyramids.	
V	Broad	Small pyramids, paler than those of III.	
VI		Pale polymorphous cells.	This area is agranular. A light line between V and VI is indicated.
<i>Area z'.</i>			
I			
III	Very narrow....	Deep pyramids.	
IV	2 or 3 × III....	Non-inflated granules.	
V	Broader than III + IV.	Deep pyramids and many inflated cells.	
VI	= IV....	Deep, round cells.	
<i>Area z''.</i>			
I			
IV		Non-inflated granules.	
V	= IV....	Inflated cells and a few deep pyramids.	
VI		Deep, round cells.	
<i>Area z'''.</i>			
I			
III	= IV....	Small, deep pyramids.	
IV		Non-inflated granules.	
V	Broader than III + IV.		Similar to V of <i>z''</i> .
VI		Inflated polymorphous cells and deep, round cells.	

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Coendu prehensilis (Lacép.).

The brain of *Coendu*, a porcupine, is obvious by its bulky, square shape. This is sufficiently demonstrated by the maps (Figs. 38, 39 and 40), and Fig. 38 shows, moreover, that the olfactory tubercle is invisible on the lateral side. It is restricted to the medio-ventral side.

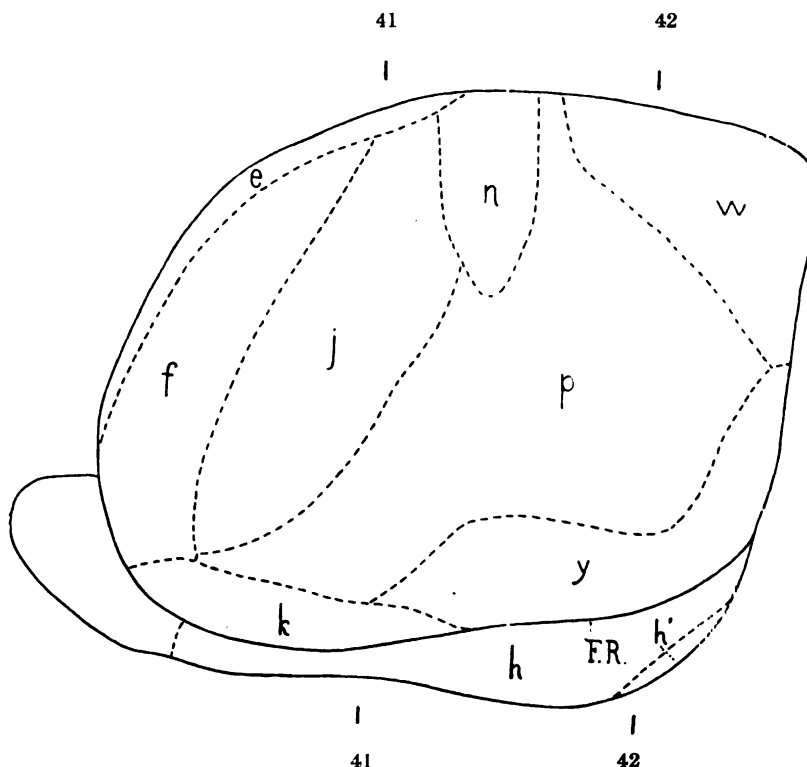


FIG. 38.—*Coendu prehensilis*. Lateral projection of the hemisphere. 4 mag. The cyphers 41 and 42 indicate the level of the sections represented by Figs. 41 and 42.

The hemispheres show many short and shallow fissures, running in all directions. But they are not constant, and the only constant fissure is again the rhinal fissure (Fig. 38, F.R.).

A series of frontal sections through the left hemisphere of one individual and a series of horizontal sections through the right hemisphere of another specimen were studied.

The brain of *Coendu* is rather simply constructed, because there are relatively few cortical areas. The greater part of these can hardly be discriminated, but my knowledge of the areas of other rodents was of great use to me.

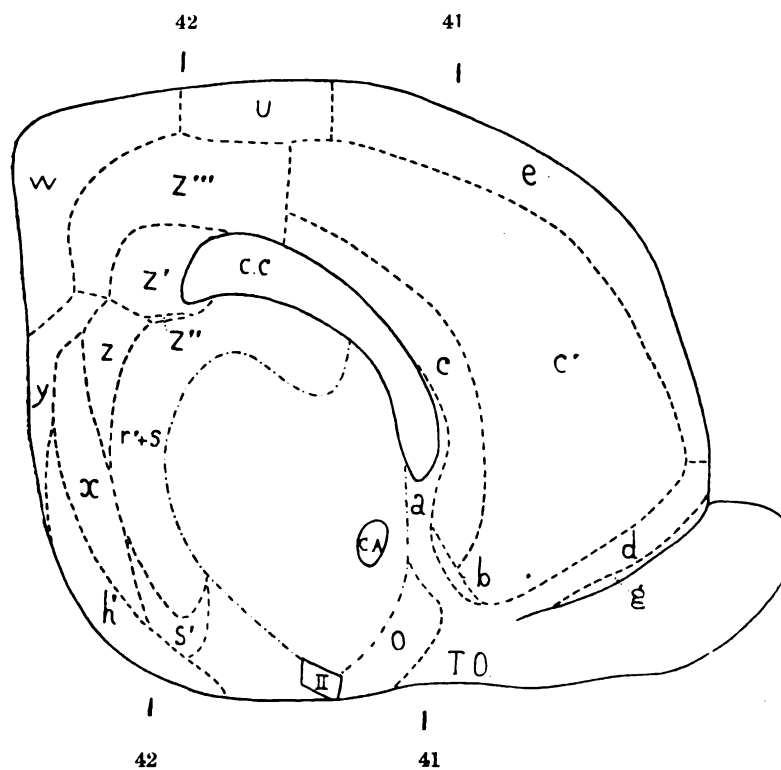


FIG. 39.—*Coendu prehensilis*. Median projection of the hemisphere. 4 mag.

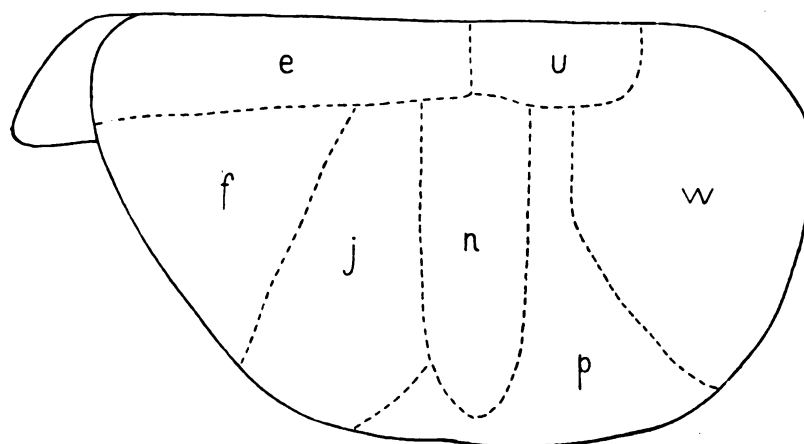


FIG. 40.—*Coendu prehensilis*. Dorsal projection of the hemisphere. 4 mag.

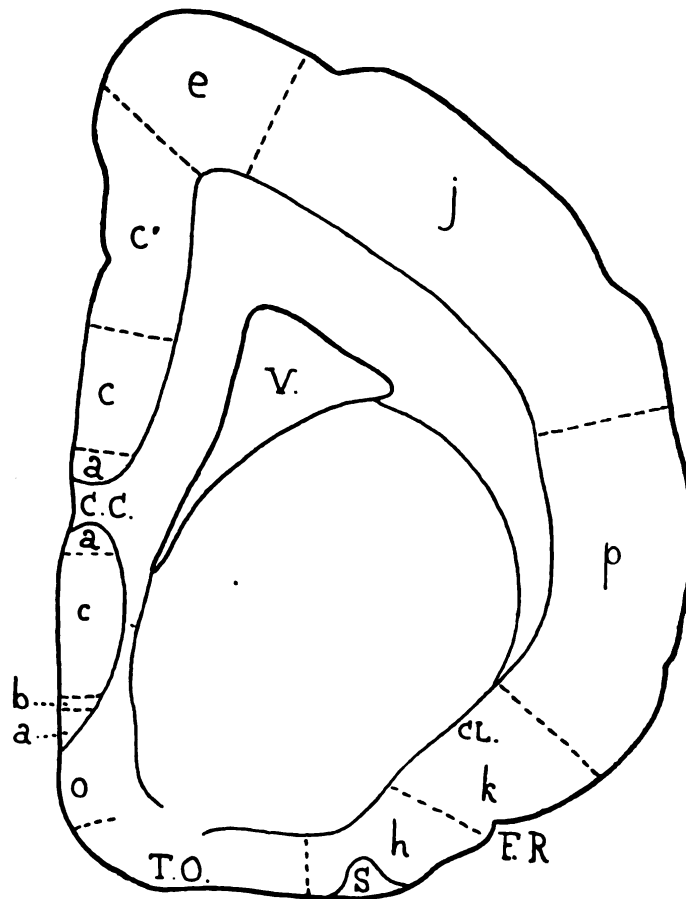


FIG. 41.—*Coendu prehensilis*. Frontal section of the hemisphere.
6 mag. Camera lucida drawing.

If, once more, one commences with beholding a frontal section through the fore-end of the corpus callosum (Fig. 41), one observes the corpus callosum to pierce an area *a*. As usual, it only consists of a layer of pyramidal cells irregularly scattered and belonging to layer V. The area embraces the genu of the corpus callosum and proceeds towards the olfactory tubercle. By the peculiar curvature of its shape it has been three times cut in the section represented by Fig. 41.

Area *b* does occur in *Coendu*, but it is very insignificant, and perhaps I would have neglected it if area *b* of *Sciurus* had been unknown to me. The extreme insignificance of it is demonstrated by Fig. 41 and the projection of the area in Fig. 39. As to its structure, it is without any doubt an area *b*, because the supra-granular pyramids are wanting, and the rather narrow

layer of inflated granules immediately joins layer I. Below layer IV is a lamina ganglionaris, which can be distinguished from layer VI by its larger and more pyramidal-shaped cells. Besides, layer V is about twice as broad as layer VI.

Dorsally and frontally of the areas *a* and *b* the areas *c* and *c'* are situated. Their extent is visible in Fig. 39. Area *c* has a layer of typical, deep supra-granular pyramids. This layer is about as broad as the granular layer, and so it is rather narrow. The granular layer is composed of inflated granules. The infra-granular pyramids below it are well developed, and the layer formed by them is about as broad as III and IV together. Undermost is layer VI, as broad as layer V, and consisting of cells of various shapes.

Area *c'* differs from *c* by its layer III being twice as broad as in area *c*, but its granular layer being narrower and indistincter. Here, too, no inflated pyramids are present. Area *c* has been twice cut in the section of Fig. 41. This fact is illustrated by Fig. 39.

The structural relation of the areas *a*, *b* and *c* can be indicated by the same scheme (Fig. 11) which I published in *Sciurus* (page 234).

At the side of area *c'* the never wanting area *d* is situated (Fig. 39). It is radiating and agranular, and runs towards the olfactory tubercle. Layer III differs little from that layer in area *c'*. Layer V is broader than in *c'*, and its pyramids are more elongated. The layer of polymorphous cells, too, is enlarged and its cells are generally pyramidal-shaped.

Area *g* in Coendu is visible on the median surface, and so it has been projected in Fig. 39. It has the well-known typical situation, *i.e.*, it occupies a portion of the ventral side of the frontal lobe of the hemisphere and proceeds backward at the bottom of the rhinal fissure. Here it soon disappears, when area *k* with the claustrum has appeared dorsally of it. Area *g* does not radiate.

The well-developed layers III and V are separated by an indistinct layer, poor in cells and representing the granular layer. Layer VI is somewhat narrower than layer V, and its cells are not pyramidal-shaped and not elongated as in the neighbouring radiating areas *e* and *d*. Area *g* can be distinguished from area *k* by the absence of the claustrum below it.

Laterally and dorsally the frontal lobe of the hemisphere is occupied by the areas *e* and *f*.

Area *f* again is tapering caudally (compare Figs. 38 and 40). Next to the zonal layer is a broad layer of small, deep supra-granular pyramids. The granular layer beneath it is three times as narrow and poor in cells. It contains round or somewhat pyramidal-shaped but always deeply-staining granules. Below this layer a very broad lamina ganglionaris is following, as broad as layer III and IV together, and endowed with many very large pyramids.

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The polymorphous layer is as broad as layer V and can be divided into two layers. A broad layer VI^a, consisting of small, rather pale-tinted pyramids, borders immediately upon layer V. Undermost is a layer VI^b, half as broad as layer VI^a. Here the cells are stellate and deeper stained and more widely dispersed than in layer VI^a.

During some time I was in doubt whether I should call the area, which is situated between *f* and *c'* and which occupies the median border of the hemisphere, area *e* or area *f'*. It differs, however, from *f* in other respects than by its radiating only. Moreover, it extends further backward than *f* and so I preferred to indicate it with the letter *e* and to homologise it with area *e* of the squirrel.

Area *e* is demonstrated by Figs. 38, 39, 40 and 41.

The lamina pyramidalis is half as broad as it is in area *f*. The granular layer is invisible or hardly visible. So, in contradistinction to area *f*, this area can be called an agranular one. The layer of infra-granular pyramids is broader than in *f*, and its cells are elongated and radiating. Moreover, they are much larger than in *f*, and approach in size the infra-granular pyramids of area *n*. The infra-granular pyramids of the frontal part of area *e* seemed to me to be smaller than those of the caudal portion. The polymorphous layer, similarly to area *f*, is divided into two layers. The cells of both layers are radiating. Both layers are equally broad, because the breadth of VI^a has been reduced to the advantage of VI^b.

Ventrally of area *f* I found area *k* with the claustrum underneath. A division into an area *k* poor in granules and an area *k'* rich in granules, could not be observed. Also, above the caudal end of the claustrum a cortex is situated, which is poor in granules and consequently must be called *k*. Area *k* is visible in Fig. 41 and its projection in Fig. 38. One must bear in mind that the area extends somewhat further in a caudal direction than has been indicated in Fig. 38, but it could not be projected in this place. The area consists of a well-developed layer of supra-granular pyramids above a narrow, indistinct granular layer poor in cells. In Coendu one cannot pretend that this layer is obvious as a light band. Layer V is obvious and has larger pyramids than layer III. Layer VI, as broad as V, has smaller, paler and rounder cells than V. Its cells are also paler than those of the claustrum, which is about as broad as V and VI together.

The frontal part of area *k* is separated by area *g* from area *h*, but the posterior part immediately borders upon area *h*. Area *h* more deviates from the homologous area in other rodents by its position than by its structure. It has more than usually been pushed ventrally of the hemisphere, which renders its projection rather narrow (Fig. 38). As in other rodents it consists

of a layer of supra-granular pyramids closely crowded together. Below these some scattered cells follow, which compose an indistinct polymorphous layer undermost. Any indication of inflated pyramids and consequently of an area h'' was wanting.

Area h has been indicated in Figs. 41 and 42; its projection is demonstrated by Fig. 38. It proceeds very far in a caudal direction and there passes into area h' (Figs. 38, 39 and 42). This area has once more its supra-granular pyramids arranged in groups. A broad layer with scattered cells follows underneath. Next to this are two narrow layers V and VI. They are often very indistinct. The former differs by its larger and deeper cells from the latter.

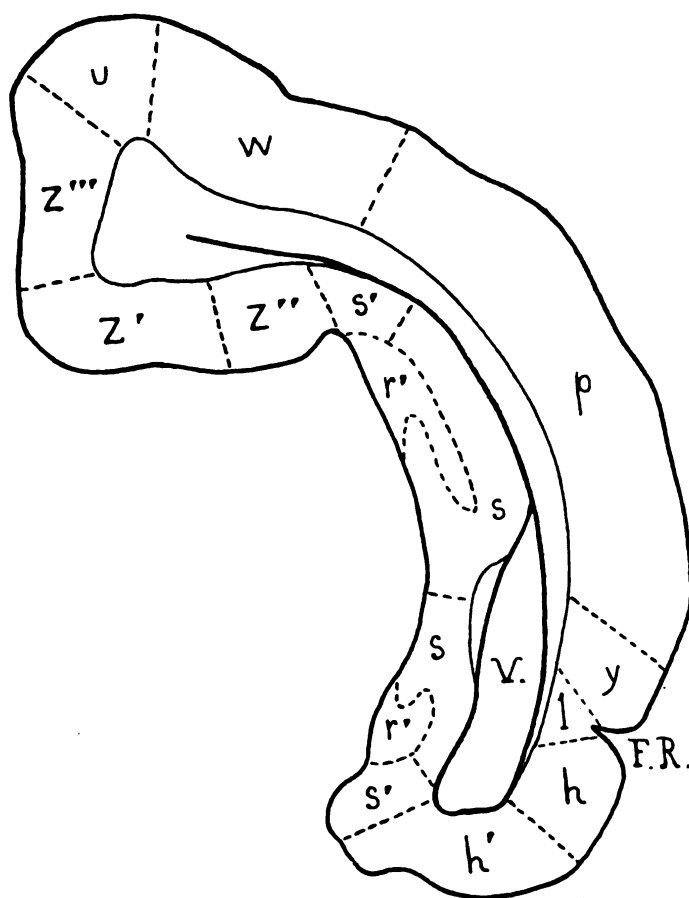


FIG. 42.—*Coendu prehensilis*. Frontal section of the hemisphere.
6 mag. Camera lucida drawing.

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Area *j* is situated caudally of area *f*, as will be illustrated by Figs. 38, 40 and 41. As to its structure it is distinguished by the breadth of its granular layer and the abundance of its granules. This layer is more than twice as broad as in area *f*, and rich in deeply-staining, more or less stellate granules. Layer III differs little from III of area *f*. Layer V is narrower and its pyramids are smaller than the infra-granular pyramids of area *f*. The polymorphous layer quite agrees with that layer in area *f*. It is divided into two layers VI^a and VI^b.

Area *n*, situated posterior to area *j* (compare Figs. 38 and 40), is obvious by the gigantic size of some of its infra-granular pyramids. They are the largest ones possessed by Coendu, and the homologisation of area *n* with the *n*-areas of other rodents is quite certain. Layer III shows none or only a few differences from that layer in *j* or *p*. The granular layer is narrower than in area *j*, but it is still rich in granules, which assume a rounder shape than in area *j*. Layer IV is much distincter than in area *p*, although the structural agreement is rather important. The ganglionic layer has a very variable breadth. At the bottom of the little fissures of the hemisphere it has been more reduced than the other layers. Layer VI shows the beginning of the described division into two layers. It also contains more pyramidal cells than in area *j*.

Area *p* occupies again a large portion of the lateral side of the hemisphere, as the Figs. 38, 40, 41 and 42 are demonstrating. Perhaps layer III is somewhat broader than in area *j*, but in other respects it is similarly constructed. It is obvious that the granular layer is narrower than in *j* and possesses less granules. Besides, this layer is indistincter, because many of its cells have the shape of small pyramids. Layer V does not differ from that of area *j*. The polymorphous layer, the cells of which are stellate, is indistinctly divided into two layers VI^a and VI^b. No dimorphy could be observed in this area. Compare for the structure of this area Plate II, Fig. 7.

Ventrally area *p* is limited partly by area *k*, partly by area *y*. This latter area is particularly large in Coendu. Area *y* is radiating and agranular. The layer of supra-granular pyramids differs little from that of area *p*. The infra-granular pyramids immediately follow below them. They are somewhat larger than the supra-granular pyramids, and can be distinguished from them by this character. In many places they are elongated, but the radiation of the area is relatively unimportant. Layer V is narrower than layer III. Layer VI is about as broad as layer III and chiefly consists of small, sometimes elongated, pyramidal cells. I am quite sure that a division into two layers VI^a and VI^b is wanting. So, this character too can be useful in determining the limit between the areas *p* and *y*. Area *y* principally extends at the side of the rhinal fissure, but it never reaches the bottom of this fissure (compare Figs. 38, 39 and 42).

The bottom of the rhinal fissure is occupied by a small area *l*, compactly constructed. Its projection is overlapped by those of other areas and so I could only indicate it in Fig. 42. It appears caudally of area *k* and proceeds towards the posterior end of the rhinal fissure. The supra-granular pyramids of this area are united into a narrow layer. I prefer to call them inflated pyramids, because they are especially pale and round. A granular layer is absent. The infra-granular pyramids accept a deeper stain than the supra-granular ones. They are lying in a broader layer than layer III and are separated from the narrow polymorphous layer by a narrow band, poor in cells.

Area *u* does occur in Coendu, but it is small and can only with some trouble be distinguished from area *w*. Area *u* is visible in Figs. 39, 40 and 42. It borders upon area *e*, but is easily distinguished from it by the absence of the giant pyramids in the lamina ganglionaris. Similarly to area *e*, area *u* is radiating. Layer III is narrow, narrower than in *w* or *p*. Layer IV is nearly as broad as layer III, but it is extremely indistinct, because most of its cells are pale-tinted pyramids and no granules. In this respect this layer agrees with layer IV of area *w*. The paler tint and the somewhat smaller size are the only characters by which one can discriminate the cells of layer IV from supra- or infra-granular pyramids.

Layer V is broader than III and IV together, and its cells surpass those of other layers in size and in deepness of colour. Layer VI is distinctly subdivided into two layers. Layer VI^a is one and a half times as broad as layer VI^b, and its cells have a paler tint. In both layers the cells are elongated, which renders them radiating.

Area *w* is again occupying the occipital lobe of the hemisphere (Figs. 38, 39, 40 and 42). Its structure is indistinct. Layer III differs not from that of area *p*. The granular layer is narrow, twice or three times as narrow as layer III. It is indistinct, because its cells are pyramidal-shaped, only somewhat smaller and paler than the pyramids of the layers III or V. Layer V is narrower than in area *p*, but also narrower than layer III. The pyramidal cells are larger and deeper than those of layer III. The polymorphous layer is broad and differs little from that of area *p*.

In Coendu, too, an area *x* is not wanting. It is totally situated on the median side (Fig. 39), but it has the well-known structure, be it not as distinctly as possible. Layer IV, poor in cells and consequently pale-tinted, is obvious. The supra-granular pyramids lie above it. They are scarcely arranged into two layers III^a and III^b, but, indeed, the pyramids are larger as they are nearer to the zonal-layer. The difference between the layers V and VI can hardly be detected. In my opinion layer V is very narrow, being no more

than a single row of cells. Its cells are somewhat larger than those of layer VI.

The structure of the areas, which area called fascia dentata and cornu ammonis, is also known to us. The fascia dentata has non-inflated granules and therefore must be indicated by r' . The cornu ammonis is called area s as in other rodents. In the neighbouring transitional area s' the non-inflated pyramids are wider dispersed. Area s' has been projected in Fig. 39 and is also visible in Fig. 42. The areas r' and s have been projected together in Fig. 39. They also have been cut in the section represented by Fig. 42.

Finally, posterior to the corpus callosum the group of z areas (z , z' , z'' and z''') is situated. Their structure in Coendu is not very characteristic. Yet, they can be homologised with the z -areas of other rodents, because their mutual differences are the same.

Area z'' (Figs. 39 and 42) has a rather broad layer of supra-granular pyramids, but this is narrower than in area c' . The granular layer is narrower than III and its granules are not inflated, as they are in c or c' . Layer V is particularly rich in cells. Consequently area z'' of Coendu lacks a character of this area in other rodents, viz., the wide dispersion of the infra-granular pyramids. Layer VI is as broad as IV and V together. It indistinctly shows a division into two layers VI^a and VI^b as found already in other areas.

Area z' (Figs. 39 and 42) embraces the splenium of the corpus callosum. It differs from area z'' by the lamina pyramidalis being about three times narrower and by the granular layer being much richer in cells.

Area z (Figs. 39 and 42) is very small in Coendu and can hardly be projected. Its structure is very indistinct, because the infra-granular pyramids are small and pale-tinted. Therefore they resemble the cells of the polymorphous layer or even granules. In this area, too, layer VI is divided into two layers. Both are about equally broad, but layer VI^b is poorer in cells than VI^a. Area z can be recognised at once by the absence of the third layer or lamina pyramidalis.

The last area which remains to be described is area z . This area, too, is very vaguely constructed but, besides by its situation (Figs. 39 and 42), it can be recognised by the absence of granules. The supra- and infra-granular pyramids can scarcely be distinguished from one another, and moreover, it is difficult to trace the limit of the layers V and VI. Properly speaking, the whole cortex of this area is composed of small pyramids. A division of layer VI is just indicated.

Coendu prehensilis.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
Area a.			
I	Irregularly arranged cells.
V	Pyramids	
Area b.			
I	Larger and more pyramids than in VI.
IV	Narrow	Inflated granules.	
V	2 × VI	Larger and more pyramids than in VI.	
VI	
Area c.			
I	Cells of various shapes.
III	Narrow	Typical, deep pyramids.	
IV	= III	Inflated granules.	
V	= III + IV	Well-developed pyramids.	
VI	= V	Cells of various shapes.	
Area c'.			
I	This layer is indistincter than in c.
III	= 2 × III of c	Typical pyramids.	
IV	Narrower than IV of c.	Similar to VI of c.
V	Typical pyramids.	
VI	
Area d.			
I	Similar to III of c'.
III	
V	Broader than V of c'	Elongated pyramids.	This area is radiating and agranular.
VI	Broader than VI of c'.	Pyramids.	
Area e.			
I	This area is agranular and radiating.
III	$\frac{1}{2} \times III$ of f	
V	Broader than in f	Elongated pyramids	
VI ^a	= VI ^b	
VI ^b	
Area f.			
I	Cells wider dispersed than in VI ^a .
III	Broad	Small, deep pyramids.	
IV	$\frac{1}{2} \times III$	Deep granules	
V	= III + IV	Many large pyramids.	
VI ^a	VI ^a + VI ^b = V	Small, pale pyramids.	
VI ^b	$\frac{1}{2} \times VI^a$	Stellate, deep cells	

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area g.</i>			
I	Indistinct and poor in cells.
III	Well-developed pyramids.	
IV	
V	Well-developed pyramids.	
VI	Narrower than V	Polymorphous cells.	
<i>Area h.</i>			
I	This layer is indistinct.
III	Pyramids crowded together.	
IV	Some scattered cells.	
VI	
<i>Area h''.</i>			
I	Cells grouped. Few scattered cells.
III	Pyramids	
IV	Broad	
V	Narrow	Larger and deeper cells than in VI.	
VI	Narrow	
<i>Area j.</i>			
I	Similar to III of <i>f</i> .
III	
IV	2 × IV of <i>f</i>	Many deep, stellate granules.	
V	Narrower than V of <i>f</i>	Smaller pyramids than in <i>f</i> .	
VI ^a	
VI ^b	Similar to VI ^a of <i>f</i> . Similar to VI ^b of <i>f</i> .
<i>Area k.</i>			
I	Indistinct and poor in cells.
III	Broad	Pyramids.	
IV	Narrow	
V	Larger pyramids than in III.	
VI	= V	Small, pale, round cells.	
Clastrum	= VI × V	Deeper cells than in VI.	
<i>Area l.</i>			
I	This area is agranular. Between V and VI is a narrow band, poor in cells.
III	Narrow	Inflated pyramids.	
V	Broader than III	Deep pyramids.	
VI	Narrow	

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area n.</i>			
I	Similar to III of <i>j</i> or <i>p</i> .
III	
IV	Narrower than in <i>j</i>	Many round granules.	
V	Very variable	Giant pyramids and smaller ones.	This layer vaguely shows a division into two layers.
VI	More pyramids than in <i>j</i> .	
<i>Area p.</i>			
I	Similar to III of <i>j</i> .
III	Broader than in <i>j</i>	
IV	Narrower than in <i>j</i>	Less granules than in <i>j</i> and these are often pyramidal shaped.	
V	Similar to V of <i>j</i> .
VI _A	Stellate cells	No great difference between VI and VI _B .
VI _B	Stellate cells	
<i>Area r'.</i>			
I	Cells crowded together. Some scattered cells beneath IV. This area is fascia dentata.
IV	Non-inflated granules.....	
<i>Area s.</i>			
I	Cells crowded together. This area is cornu ammonis.
V	Narrow	Typical pyramids	
<i>Area s'.</i>			
I	Cells more dispersed than in <i>s</i> .
VI	Typical pyramids	
<i>Area u.</i>			
I	Narrower than in <i>p</i> or <i>w</i> . Very indistinct
III	Narrow	Deep pyramids	
IV	= IV.....	Generally small pale pyramids.	No giant pyramids.
V	Broader than III + IV.	Deep large pyramids	
VI _A	1½ × VI _B	Paler cells than in VI _B	Cells elongated. Cells elongated. This area is radiating.
VI _B	
<i>Area w.</i>			
I	Similar to III of <i>p</i> .
III	
IV	½ × III	Pyramidal cells but smaller and paler cells than in III or V.	
V	Narrower than in <i>p</i>	Larger and deeper pyramids than in III.	Similar to VI of <i>p</i> .
VI	Broad	

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area x.</i>			
I
III	Pyramids	Scarcely divided into IIIA and IIIB.
IV	Poor in cells and pale tinted.
V	Very narrow....	Pyramids	Only one row of cells.
VI	Small cells than in V.
<i>Area y.</i>			
I
III	Similar to III of <i>p</i> . Often elongated.
V	Narrower than III	Larger pyramids than in III.
VI	= III	Small elongated pyramids.	Not divided into VIA and VIB.
			This area is agranular and radiating.
<i>Area z.</i>			
I
III	Small pyramids.
V	Small pyramids.
VI	Small pyramids.	The layers can hardly be distinguished.
<i>Area z'.</i>			
III	$\frac{1}{2} \times$ III of <i>z'''</i>
IV	Non-inflated granules....	More cells than in IV of <i>z'''</i> .
V
VI	In other respects this area is similar to <i>z'''</i> .
<i>Area z''.</i>			
I
IV	Granules.
V	Small and pale pyramids.	Resembling polymorphous cells.
VIA	= VIB
VIB	Poorer in cells than VIA.
<i>Area z'''.</i>			
I
III	Broad	Pyramids.
IV	Narrower than III	Non-inflated granules.
V	Pyramids	Rich in cells.
VI	= IV + V	Indistinctly divided into VIA and VIB.

Dipodomys merriami nitratoides.

The brain of *Dipodomys* greatly resembles the brain of the mouse, although both animals belong to different families. The size and external shape of both brains is nearly the same, and a remarkable point of agreement is the absence of a rhinal fissure in the posterior half of the hemisphere (Fig. 43). No fissures besides the very short rhinal fissure are present.

I studied two brains of *Dipodomys*. One of them was cut into a series of frontal sections, the other one was cut horizontally.

The genu of the corpus callosum pierces area a' as in the mouse. This area only embraces the genu as a narrow band (Figs. 44 and 46) and never has the breadth of the ventral portion of area a' in the mouse. Consequently its structure is nowhere distinct. In the whole area the corpus callosum has reduced the layers III, IV, V and VI, which it ought to have, to a single narrow layer of deep pyramids. Yet, I will homologise this area with area a' of the mouse on account of its deeply staining zonal layer, and because it is quite similar to that part of area a' in the mouse, which immediately surrounds the corpus callosum.

Area a is only small in *Dipodomys*. As usual, its cortex passes into the cortex of the olfactory tubercle without a definite limit (Fig. 44). It only consists of a layer of deeply staining pyramids which must be considered infra-granular pyramids.

Between the areas a' and a I found an area, which on account of its structure could not be homologised with any other area. I will call it a'' . Area a'' occupies the place of a portion of area a' in the mouse (Fig. 44), but its structure differs from area a' , as well as from area a'' . It has no granular layer and no deeply staining zonal layer as a' has, and it is endowed with supra-granular pyramids, which are absent in area a'' . Area a'' is composed of a narrow layer of small deep supra-granular pyramids. Below this, a lamina ganglionaris follows, twice as broad as layer III. Its cells are much wider dispersed than the cells either of III or of VI. The cells of the polymorphous layer, which is as broad as layer III, are rounder than the short pyramids of V. Area a'' is also indicated in Fig. 46.

Dorsally and in front of the areas a' and a'' I observed an area with a complete cortex; area c (Figs. 44 and 46). The pyramidal layer is narrow, and has small deep pyramids. The granular layer is indistinct and can chiefly be recognised by the paler tint of its cells. It is about as broad as layer III. The ganglionic layer has a variable breadth. It has larger pyramids than layer III and is rather distinct. The polymorphous layer contains, besides

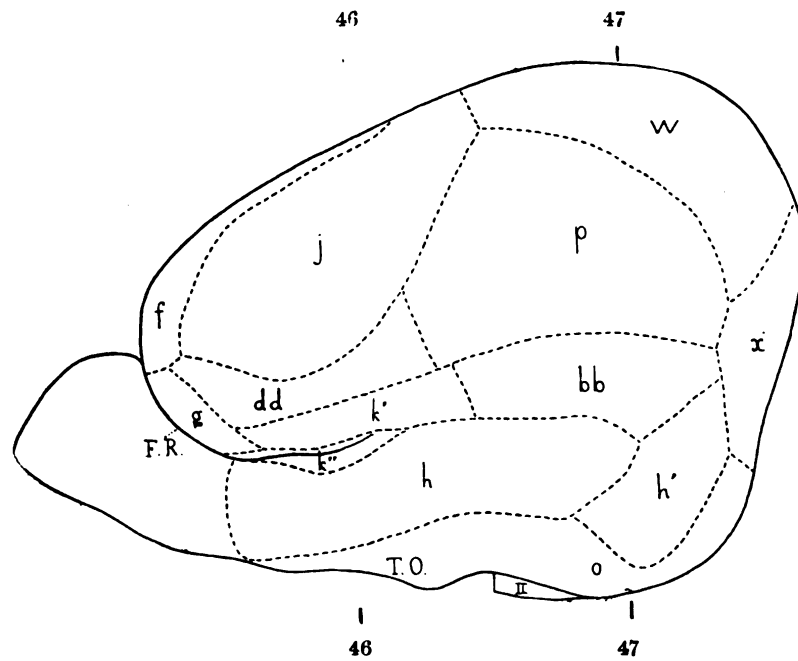


FIG. 43.—*Dipodomys merriami nitratoides*. Lateral projection of the hemisphere. 5 mag. The ciphers 46 and 47 indicate the level of the sections represented by Figs. 46 and 47.

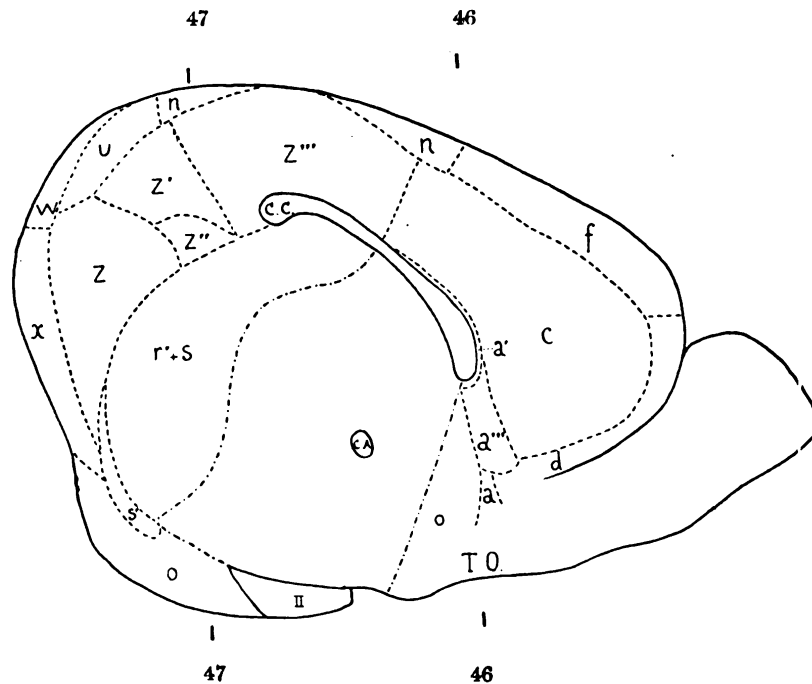


FIG. 44.—*Dipodomys merriami nitratoides*. Medial projection of the hemisphere. 5 mag.

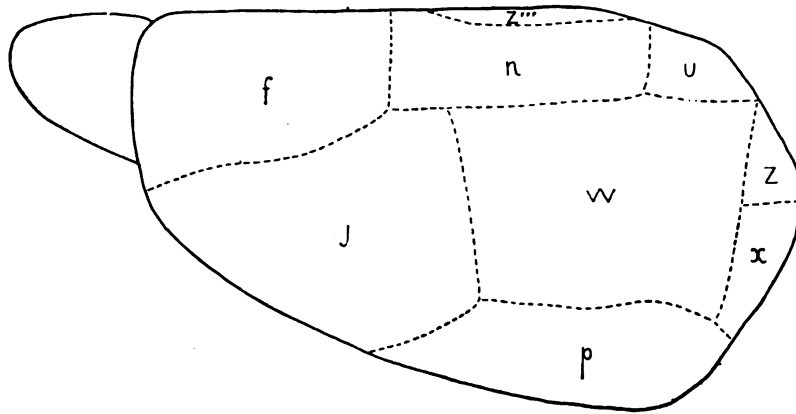


FIG. 45.—*Dipodomys merriami nitratoideus*. Dorsal projection of the hemisphere. 5 mag.

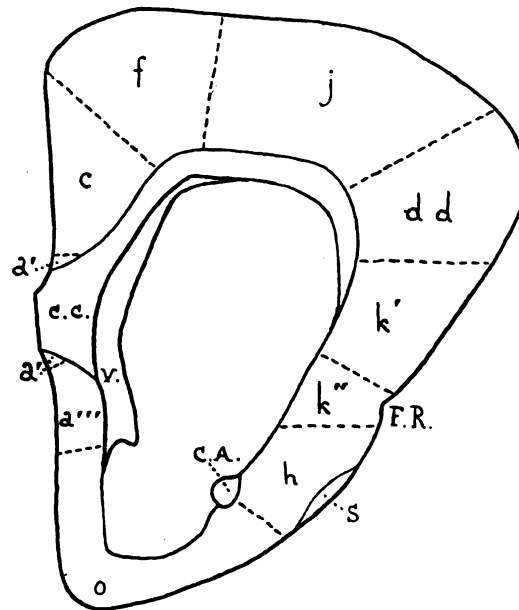


FIG. 46.—*Dipodomys merriami nitratoideus*. Frontal section of the hemisphere. 15 mag. Camera lucida drawing.

small pyramids, cells of other shapes. It is broadest in the most dorsal parts of the area.

Area *d* is agranular and radiating. All cells of the layers III, V and VI are elongated, those of the layers III, and VI being small, those of layer V large pyramids. Area *d* occupies the well-known position, visible in Fig. 44.

Area *f* immediately borders upon area *c*. Consequently the areas *f'* or *e* are absent in *Dipodomys*. Layer III of *f* is well developed and about as broad
(16147)

as III + IV of *c*. Its pyramids are small. The granular layer is very indistinct, only consisting of a few rows of pale round cells. It is even narrower than in *c*. The deep infra-granular pyramids are lying in a broad layer, as broad as layer III and IV together. The cells of the polymorphous layer are smaller and rounder than the infra-granular pyramids. The layer itself is about as broad as layer V. Area *f* is visible in Figs. 43, 44, 45 and 46.

Laterally of area *f*, area *j* is situated. In *Dipodomys*, too, it is obvious by the large quantity of cells in the granular layer. These cells are deep, non-inflated granules. The layer of supra-granular pyramids is particularly well-developed in this area. It is still broader than III of *f*. The granular layer is only somewhat narrower than III. Compared with area *f* the layer of infra-granular pyramids has been greatly reduced in area *j*. It is narrower than the granular layer, but it has also large deep pyramids, similarly to layer V of *f*. The polymorphous layer is divided into two layers VI^a and VI^b. In VI^b, which is very narrow, only $\frac{1}{2}$ of VI^a, the cells are closer crowded together. In both layers they are deep, polymorphous cells.

In contradistinction to the other rodents described in this paper, area *j* does not border ventrally upon area *k* or *k'*, but upon an area without claustrum underneath. As I could not find its homologue in other rodents I will call it area *dd*. Area *dd* has been projected in Fig. 43 and has also been indicated in Fig. 46. Area *dd* obviously differs from area *j* by its having less granules. From area *k'* it chiefly differs by the larger infra-granular pyramids which belong to a broader and distincter layer and by the absence of the claustrum. Layer III is about as broad as IV, but both layers are narrower than in *j*. The granules are deep, non-inflated granules composing a rather indistinct granular layer. The Vth layer is similar to V of area *j*. Its infra-granular pyramids are well developed and rather widely dispersed. The polymorphous layer is very broad but not divided into two layers.

The claustrum runs below two cortical areas *k'* and *k''*. Area *k'* is situated dorsally of area *k''* (compare Figs. 43 and 46), and it never reaches the bottom of the rhinal fissure. It has a complete but rather indistinctly constructed cortex. Layer III is somewhat narrower than III of *dd*, but in other respects it is similar to it. The granules in the granular layer are about as numerous as they are in *dd*. On the other hand the infra-granular pyramids have diminished in size compared with those of *dd*, and the Vth layer has become narrower. The polymorphous layer is about as broad as layer V, and it lacks the many pyramids of this layer in area *dd*. The claustrum consists of spindle-shaped cells, staining deeper than the polymorphous cells. It is narrower than layer VI.

Area *k'* occupies the bottom of the rhinal fissure, but also extends ventrally of it. On account of this character, and on account of the extreme poverty in cells of the granular layer, I am obliged to homologise it with area *k''* of the mouse. Yet, the infra-granular pyramids, which formed a very narrow layer in the mouse, are totally wanting in *Dipodomys*. The supra-granular pyramids of area *k''* are larger than in *k'* and they are crowded together. By both these characters this layer resembles the IIIrd layer of area *h*. The lamina pyramidalis lies above a layer nearly free from cells and contrasting as a light band. This layer represents the granular layer, perhaps also layer V, which is wanting in this area. The polymorphous layer and the claustrum resemble those of area *k'*. Area *k''* is indicated in Figs. 43 and 46.

Laterally the ventral part of the frontal lobe of the hemisphere is occupied by area *g*. This area is visible in Fig. 43. It is not radiating and differs in this respect from area *d*. The layer of supra-granular pyramids is narrow, half as broad as that layer in area *f*. The cells in it are more numerous and deeper stained than the granules in the granular layer. But for this, both layers would be quite similar, as in both the cells are small pyramids and round cells. The ganglionic layer is obvious by its large, deep pyramids. Below this follows the polymorphous layer, as broad as III, IV and V together, and composed of cells of various shapes, but not so deeply staining as the infra-granular pyramids do.

Area *h* is present in its ordinary place (Figs. 43 and 46) and possesses the well-known structure. The deeply staining pyramids of layer III are closely crowded together and they lie above a layer poor in cells, representing layer IV. Below this the cells are again more numerous and form a polymorphous layer. Their shape is rounded in layer VI.

Area *f* passes in a caudal direction into area *n*. This area is remarkable for the giant pyramids of its ganglionic layer, and it is on account of this that I homologise it with the *n*-areas of other rodents. Another point of interest is its layer of supra-granular pyramids. Here the cells are extraordinary small and polygonal. So, they greatly resemble the granules of other areas, but the granules of area *n* itself are perfectly round and still smaller than the supra-granular pyramids. By these qualities one can distinguish layer III from layer IV, and then layer IV appears to be somewhat broader than III. Layer V is broader than III and IV together, and the large pyramids in it are widely dispersed. The polymorphous layer is about as broad as layer V. Its cells are small pyramids and cells of various shapes. The layers V and VI can be somewhat radiating, especially in the caudal end of the area. Area *n* is visible in Figs. 44, 45 and 47.

In area *w* the layers III and IV can hardly be separated. I would say,

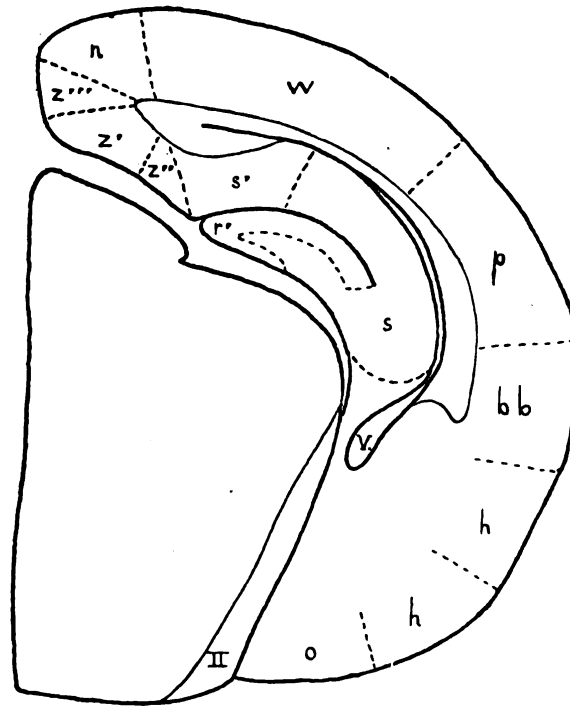


FIG. 47.—*Dipodomys merriami nitratoideus*. Frontal section of the hemisphere.
15 mag. Camera lucida drawing.

that the only difference between them is the fact that the granules are somewhat smaller than the supra-granular pyramids. The granules are not so numerous as in area *j*, but more numerous than in *p*. The layers III and IV are together about as broad as the layers V and VI together. Layer V, about as broad as layer VI, has well-developed deep pyramids, but they are not as large as in area *n*. The polymorphous layer consists of small cells of various shapes, which undermost are arranged in rows parallel to the myelum. Area *w* is visible in Figs. 43, 44, 45 and 47.

Area *p* generally resembles area *w*, but the difference between the layers III and IV is more obvious. The supra-granular pyramids, although small, are somewhat larger than in area *w*, and the granules are less numerous. I found layer III somewhat broader than IV. The layers V and VI are similar to those of *w*. Consequently, they differ from those of the neighbouring area *bb*, which has more but paler infra-granular pyramids and no polymorphous cells arranged in parallel rows. Area *p* has been projected in Figs. 43 and 45. It is also visible in Fig. 47, and Plate II, Fig. 9, demonstrates its structure.

Dipodomys is endowed with an area *bb*, like the mouse. As in both these

animals the rhinal fissure is absent in this region, and as area *bb* does not occur in the other described rodents, I am convinced that the absence of the rhinal fissure is one of the causes of development of area *bb*. Area *bb* has generally pale cells. The layer of supra-granular pyramids is rather broad and its cells more or less grouped. The granular layer is not absent, as it was in the mouse, but it is poor in cells. This layer is narrower than layer III or V. The layer of infra-granular pyramids is about as broad as layer VI. Its cells are somewhat more numerous than in area *p*, but besides that it has nothing peculiar. The polymorphous layer has its cells not arranged into parallel rows, as in area *p*. Area *bb* is visible in Figs. 43 and 47.

Posterior to the areas *h* and *bb* I observed area *h'*. In many respects it resembles area *h*, but its deep supra-granular pyramids are grouped and the polymorphous layer is not everywhere obvious. Area *h'* has been drawn in Figs. 43 and 47.

Area *x* too could be observed in the *Dipodomys*. Its situation in the posterior part of the hemisphere is demonstrated by Figs. 43, 44 and 45. Its layer of supra-granular pyramids is broad, but, although the cells near the zonal layer are larger than the inferior ones, it is not obviously divided into two layers III^a and III^b, as in other rodents. Moreover, the supra-granular pyramids are not grouped. Layer III is followed by a narrow fourth layer, free or nearly free from cells. This layer contrasts as a light band. Layer V is as broad as layer IV and consists only of one or two rows of large cells, more polygonal than pyramidal shaped. The polymorphous layer is broader than V and built up of small round cells.

Area *u* succeeds area *n* in a caudal direction. It differs from *n* by the want of giant pyramids in the ganglionic layer. Moreover, it is radiating. In area *u* every trace of difference between the layers III and IV is absent. All cells above the infra-granular pyramids are small, deep, round cells, *i.e.*, they perfectly have the shape of non-inflated granules. Yet, I am not inclined to declare the layer of supra-granular pyramids to be absent. Firstly, on account of the apparent homology of this area with the *u* areas in other rodents, where a IIIrd layer is present. And secondly, because in the neighbouring area *w* the difference between supra-granular pyramids and granules is so slight, that here too a very unimportant change is needed to render them quite similar to one another. The layers III and IV are together twice as broad as the ganglionic layer. This layer is similar to V of area *w*. The polymorphous layer differs only by its radiating from that layer in area *w*. Area *u* has been projected in Figs. 44 and 45.

The cornu ammonis and fascia dentata have been projected together in Fig. 44 (*r'* + *s*). The fascia dentata (area *r'*) consists of a layer of non-

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inflated granules closely crowded together. As always some scattered stellate cells lie beneath them. The cornu ammonis only consists of a layer of deeply staining infra-granular pyramids. These too are closely packed up. The areas *r'* and *s* have been also indicated in Fig. 47.

The existence of a transitional area *s'*, where the infra-granular pyramids are wider dispersed, is demonstrated by Figs. 44 and 47.

The group of *z*-areas, which remains to be described, occupies a crescent-shaped place on the median side of the hemisphere. Their somewhat distorted projection is visible in Figs. 44 and 45, and the areas *z'*, *z''* and *z'''* are visible in the section represented by Fig. 47. I found the structure of the *z*-areas homologous with that in other rodents, but the cells of the layers III and IV more than usually resembled one another.

Area *z'''*, extending above the corpus callosum, has a narrow layer of small round cells, representing the supra-granular pyramids. But the granular layer underneath is still narrower and its cells are still smaller and not so numerous as in layer III. The layer of infra-granular pyramids is twice as broad as III and IV together, and its cells are large deep pyramids, rather widely dispersed. The polymorphous layer consists of small cells.

In area *z''* the supra-granular pyramids are wanting. The layers IV, V and VI are about equally broad, layer IV consisting of small deep granules, layer V of rather small pyramids, and the polymorphous layer of widely dispersed small cells.

Area *z'* only differs from *z''* because the proportion of the breadth of the layers III and IV is reversed. The granular layer of *z'* is about twice as broad as its lamina pyramidalis.

Area *z* is agranular. A narrow layer of very small supra-granular pyramids is immediately followed by a somewhat broader layer of larger pyramids. Under most is a polymorphous layer with cells of various shapes and broader than III and V together. Between the layers V and VI is a narrow but obvious light band.

Dipodomys merriami nitratoides.

(Table of characterising histological details.)

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area a.</i>			
I			
V		Deeply staining pyramids.	

Layer.	Breadth.	Cells.	Further Remarks.
I III + IV + V + VI	Narrow	Area a'. Deep pyramids.	Deeply staining. Everywhere the corpus callosum compresses the layers III, IV, V and VI.
I III V VI	Narrow 2 × III = III	Area a'''. Small deep pyramids. Short pyramids Round cells.	Cells wider dispersed than in III or VI. This area is agranular.
I III IV V VI	Narrow = III Variable Variable	Area c. Small deep pyramids. Pale cells Larger pyramids than in III. Small pyramids and cells of other shapes.	This layer is indistinct.
I III V VI		Area d. Small elongated pyra- mids. Large elongated pyra- mids. Small elongated pyra- mids.	This layer is agranular and radiating.
I III IV V VI	= III + IV of c Narrower than in c = III + IV = V	Area f. Small pyramids. Pale round granules Deep pyramids. Smaller and rounder cells than the pyra- mids of V.	Only a few rows of cells.
I III IV V VI	$\frac{1}{2} \times$ III of f = III + IV + V	Area g. More and deeper stain- ing cells than in IV. Small pyramids and round cells. Large deep pyramids. Polymorphous cells, paler than those of V.	
I III IV VI		Area h. Deep pyramids, closely crowded together. Very few cells. Rounded cells.	

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Layer.	Breadth.	Cells.	Further Remarks.	
<i>Area h'.</i>				
I	This layer can be wanting. In other respects this area is similar to area <i>h</i> .	
III	Deep pyramids, arranged in groups.		
IV		
VI		
<i>Area j.</i>				
I	Cells closer crowded than in VIA.	
III	Broad	Deep pyramids.		
IV	Narrower than III	Many non-inflated granules.		
V	Narrower than IV	Large deep pyramids.		
VIA	Deep polymorphous cells.		
VIB	$\frac{1}{2} \times VIA$		
<i>Area k'.</i>				
I		Similar to III of <i>dd</i> .
III	Narrower than III of <i>dd</i>		
IV	Granules	Cells about as numerous as in IV of <i>dd</i> .	
V	Narrower than V of <i>dd</i> .	Pyramids	Smaller cells than in V of <i>dd</i> .	
VI	= V	Polymorphous cells.	Cells deeper stained than those of VI.	
Clastrum	Narrower than VI	Spindle-shaped cells		
<i>Area k''.</i>				
I	Cells crowded together.	
III	Larger pyramids than in III of <i>k'</i> .		
IV	Very few cells	This layer forms a light band. Similar to VI of <i>k'</i> . Similar to the claustrum in <i>k'</i> .	
VI		
Clastrum		
<i>Area n.</i>				
I	Resembling granules.	
III	Extraordinary small polygonal cells.		
IV	Broader than III	Perfectly round granules	Smaller than the cells of layer III. Pyramids dispersed.	
V	Broader than III + IV.	Large and giant pyramids.		
VI	= V	Small pyramids and polymorphous cells.	The layers V and VI are sometimes radiating.	
<i>Area p.</i>				
I		Cells somewhat larger than in III of <i>w</i> .
III	Broader than IV	Small pyramids		
IV	Granules	Less granules than in IV of <i>w</i> .	
V	Similar to V of <i>w</i> .	
VI	Similar to VI of <i>w</i> .	

Layer.	Breadth.	Cells.	Further Remarks.
<i>Area r'.</i>			
I
IV	Non-inflated granules....	Closely crowded together. Some scattered stellate cells beneath the granules. This area is fascia dentata.
<i>Area s.</i>			
I
V	Deeply staining pyramids.	Cells crowded together. This area is cornu ammonis.
<i>Area s'.</i>			
I
V	Similar to V of <i>s</i> , but the pyramids are wider dispersed.
<i>Area u.</i>			
I
III + IV	2 × V	Small, round, deep cells	Cells resembling non-inflated granules.
V	Similar to V of <i>w</i> .
VI	Radiating but otherwise similar to VI of <i>w</i> . This area is radiating.
<i>Area w.</i>			
I
III	III + IV = V + VI	Cells resembling granules but somewhat larger.
IV	Non-inflated granules	Less granules than in <i>j</i> , more than in <i>p</i> .
V	= VI	Large deep pyramids.
VI	Small polymorphous cells.	Undermost the cells are arranged in rows parallel to the myelum.
<i>Area x.</i>			
I
III	Deep pyramids	Pyramids larger near layer I, not grouped.
IV	Narrow	Nearly free from cells.	This layer contrasts as a light band.
V	= IV	Large polygonal cells	Only one or two rows of cells.
VI	Broader than V	Small round cells.
<i>Area z.</i>			
I
III	Narrow	Very small pyramids.
V	Broader than III	Larger pyramids than in III.
VI	Broader than III + V.	Polymorphous cells.	Between the layers V and VI is an obvious, narrow, light band. This layer is agranular.

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Layer.	Breadth.	Cells.	Further Remarks.
<i>Area z'.</i>			
I	In other respects similar to <i>z''</i> .
III.....	
IV	2 × III	
V	
VI	
<i>Area z''.</i>			
I	Cells widely dispersed.
IV	= V	Small deep granules.	
V	Small pyramids.	
VI	= V	Small polymorphous cells.	
<i>Area z'''.</i>			
I	Cells less numerous than in III. Cells rather widely dispersed.
III	Narrow	Small round cells.	
IV	Narrower than III ..	Smaller cells than in III	
V	2 × III + IV	Large deep pyramids	
VI	Small cells.	
<i>Area bb.</i>			
I	Cells more or less grouped. Poor in cells.
III	Broad	Pale pyramids	
IV	Narrower than III or V.	More cells than in V of <i>p</i> . Cells not arranged in parallel rows as in <i>p</i> .
V	= VI.....	Pyramids	
VI	Polymorphous cells	
<i>Area dd.</i>			
I	Less granules than in IV of <i>j</i> .
III	= IV.....	
IV	Narrower than in <i>j</i> ..	Deep non-inflated granules.	Similar to V of <i>j</i> .
V	Large widely dispersed pyramids.	
VI	Very broad	Not divided into two layers.

GENERAL COMPARISON.

In this chapter I intend to compare my own results and draw comparisons of the same with the results obtained by other authors.

For the sake of a convenient survey I once more have published the brain-maps all together on the plates facing page 332.

In all rodents, which were studied by me, a group of areas is situated between the genu of the corpus callosum and the olfactory tubercle. I have called these areas *a*, *a'*, *a''* and *a'''*.



FR.

Area *a* always only consists of a layer of infra-granular pyramids. It is always present. Only in the mouse and the waltzing-mouse was it so indistinct that I could not indicate its definite limits. Area *a* can be (in the rabbit, the hare and Coendu) the only area of the group of *a*-areas which is present. It then embraces the genu of the corpus callosum. More often (in Sciurus, rat, mouse, waltzing-mouse, Cavia and Dipodomys) the corpus callosum is frontally surrounded by area *a'*. It is compactly constructed, but has a complete cortex. I observed area *a''* only in the genus *Mus* and area *a'''* only in *Dipodomys*.

I found area *b* in *Sciurus*, *Coendu* and the guinea-pig, but not in other rodents. It has a remarkable structure, because layer III is totally wanting. Besides it is interesting by the various degrees of its extent in the three rodents.

The anterior part of the flat median surface of the hemisphere is occupied by the areas just mentioned, also by the areas *c* and *c'*.

They have a complete cortex. Area *c* is never absent, although its extent is very variable. In the rabbit, the hare and *Coendu* area *c'* appears dorsally and frontally of it.

Area *d* is constantly present. It joins the olfactory tubercle and occupies a part of the border of the hemisphere. It is always radiating and devoid of granules, except in *Cavia* and the rabbit.

Area *f* is another area which is always present. It occupies a large portion of the frontal lobe of the hemisphere. Generally speaking, it is characterised by few granules and many large infra-granular pyramids. In the rabbit and *Dipodomys* it also occupies a portion of the median border of the hemisphere. In other rodents (rat, mouse, waltzing-mouse, hare and guinea-pig) this part has been more differentiated and has become area *f'*. This area still greatly resembles area *f'*, but it is radiating and differs in the breadth of its layers; it possesses, for instance, always less granules than area *f*. This differentiation can proceed and give rise to an area *e* in *Sciurus* and *Coendu*. This area differs by its structure and extent too much from area *f* to be suitably indicated by *f'*. Yet, I shall not be surprised if the investigation of still more rodentia leads to the detection of a gradual transition of *f* into *f'* and of *f* into *e*. In that case one will scarcely know how to indicate the median portion of area *f*. Area *f* can be dimorphous, for instance, in the rabbit.

Area *g* constantly occurs. It has the same position everywhere, as it always occupies the anterior portion of the bottom of the rhinal fissure and a part of the ventral side of the frontal lobe of the hemisphere. Its structure, however, is deviating in the rodents which I studied.

I indicated with *h* that portion of the palaeocortex, which in all rodents
(16147) 2 c

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is present ventrally of the rhinal fissure, at least of its anterior portion. It always consists of a layer of closely crowded pyramids. Some stellate cells are scattered beneath them and they can constitute in the inferior parts of the cortex a more or less distinct polymorphous layer. In the squirrel, the mouse, the waltzing-mouse, the hare, *Coendu* and *Dipodomys* the pyramidal cells are never inflated. When inflated pyramids are mixed with the non-inflated ones, the area is called $h + h''$ (*Cavia*, rat). When, as in the rabbit, the inflated pyramids are forming a separate area, this area is called h'' .

Posterior to the areas h and h'' one will always find area h' , but in one rodent it is much more distinct than in the other one. The supra-granular pyramids of this area are always grouped and sometimes, for instance, in the rabbit, layer III is divided into two layers, as in the neighbouring area x . The layers V and VI can be more or less distinctly present. The areas h , h' and h'' never contain granules.

It is obvious that area h' forms a structural transition of h into x . If it is endowed with an undivided pyramidal layer and if it lacks layer V, then it greatly resembles area h . If, on the other hand, the layers III^a, III^b and V are present, then it more agrees with area x .

Area j is a never-wanting area situated between the constant areas f and p . All layers are present, but the area is properly distinguished by its large quantities of granules. In the genus *Mus* the granular layer is clouded in a peculiar way. This is also the case with an area situated in the guinea-pig at the side of area j . I called it j' on this account. Area j is dimorphous in the squirrel and also in the genus *Mus*.

In *Coendu* the claustrum extends below a single area k , but in *Sciurus*, *Cavia* and the genus *Lepus*, below two areas k and k' . In both areas all the cortical layers are present, but the anterior area k has less granules than the posterior one k' . In the genus *Mus* no area k' occurs. Here, however, I found area k'' developed. This area extends area k in the poverty in cells of layer IV. Indeed, the granular layer is here so poor in cells that it contrasts with the neighbouring layers as a light band. Moreover, area k'' always extends ventrally of the rhinal fissure, and all its layers are narrower than in area k . In *Dipodomys* area k is absent and the areas k' and k'' are developed.

In my opinion it is quite possible that area k'' is only a part of area k , which has obtained a special structure, in connection with its extending ventrally of the rhinal fissure.

If this be so, the differentiation of area k into two areas would not yet have taken place in the guinea-pig, whereas in *Dipodomys* the whole area k would have been changed into area k'' .

The most striking point of difference in the claustrum of the various rodents was its extent below the rhinal fissure in some cases.

Area *l* is compactly constructed and occupies the bottom of the rhinal fissure posterior to the claustrum. It is present in *Sciurus*, the rat, the guinea-pig, the hare and *Coendu*; it is absent in the mouse, the waltzing-mouse, the rabbit and *Dipodomys*. Its extent is very variable.

Properly speaking, area *m* only occurs in the squirrel. Here it is distinctly distinguished from area *u* and from *m'*, which chiefly differs from *m* by its radiating structure. In other rodents, however, one observes areas which, either on account of their structure or on account of their situation, can be homologised with *m* or with *u*. Then it is doubtful whether they are better called *m* or *u*.

After careful consideration I am of opinion that in rodents the posterior part of the median border of the hemisphere and portions of its median and dorsal sides are occupied by an area which can be differentiated in more than one direction and can assume various shapes (called *u*, *m* and *m'*). These different types are more or less connected by transitions. So, I think it possible that the study of more rodents than the nine, which are described in this paper, will cause some alterations in the homologisation of these areas.

Area *n* has a complete cortex with extraordinary large infra-granular pyramids. These pyramids are the largest ones which the animal has. Area *n* is absent only in the genus *Lepus* (rabbit and hare). In the other rodents it lies posterior to the areas *f* and *j*. In the guinea-pig it goes beyond the median border of the hemisphere, and this portion is radiating (area *n'*).

To give some idea about the relation of the length of the largest infra-granular pyramids of the area *n* and *f*, I publish here some average measurements.

Average length of the largest infra-granular pyramids of :—

—	Area <i>f</i> .	Area <i>n</i> .
<i>Coendu</i>	44 μ	88 μ
<i>Hare</i>	40 μ
<i>Rabbit</i>	26 μ
<i>Squirrel</i>	30 μ	66 μ
<i>Guinea-pig</i>	26 μ	44 μ
<i>Rat</i>	22 μ	30 μ
<i>Dipodomys</i>	22 μ	26 μ
<i>Mouse</i>	18 μ	22 μ

In the table the animals are arranged according to the size of the brain. It is obvious that the difference in length between the pyramids of *f* and *n* is relatively diminishing in animals with small brains. Both rows of figures are demonstrating that the length of homologous pyramidal cells is varying greatly and more or less parallel to the size of the brain.

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With *o* I indicated all regions free from cortex.

Area *p* occurs in all rodents. It is one of the largest areas everywhere and has a complete cortex. In the squirrel, the rabbit and the guinea-pig it is dimorphous.

Area *q* is only present in *Sciurus*. I could not find its homologon in other rodents, as was also the case with other areas of *Sciurus*.

I discussed area *u* already together with area *m*. Here I will only mention that I called *u'* a portion of area *u*, which is only obvious in the hare.

None of the areas is indicated by *v*.

Area *w* again is present in all rodents. It greatly varies in its structure as well as in its extent. It is built up of all cortical layers, but the granular layer is often its most characteristic layer.

Area *x* is a constant area. It is wholly or for the greater part situated on the median side and belongs to the palaeocortex. Where the area is well developed it shows the layers III^a and III^b, then a layer poor in cells, then a layer of infra-granular pyramids and undermost a polymorphous layer. However, layer V may be absent and the layers III^a and III^b may be united into a single layer III.

If I may call the areas *h*, *h'* and *x* areas of the palaeocortex, then the structure of the palaeocortex appears to become more successively complicated in them. Thus, area *h* at least consists of a layer III with a layer poor in cells beneath it (*Lepus europaeus*), but more often a polymorphous layer is present below the layer poor in cells. Area *h'* at least consists of the layers III and VI separated by a layer poor in cells (mouse). But, layer III can be divided into III^a and III^b (rabbit), and layer V may be developed (squirrel). Finally in area *x* the layer poor in cells has much diminished in breadth and now its homology with layer IV of the neocortex is obvious. Layer III is most times divided and layer V is often developed.

The rabbit has area *x'* characterised by inflated cells.

Area *y* is present in the rabbit, the hare, the guinea-pig and *Coendu*. It is always radiating and its granular layer is poorly developed, when it is not wanting. This area accompanies the posterior part of the rhinal fissure at the dorsal side.

The areas *z*, *z'*, *z''* and *z'''* constitute a group of areas which are mutually related by their structure and are present in similar situations in the rabbit, the hare, the guinea-pig, *Coendu* and *Dipodomys*. Area *z* is agranular, area *z''* has no supra-granular pyramids, and area *z'''* has more supra-granular pyramids and less granules than *z'*. These are their principal differences.

In the rabbit area *z^{iv}* joins these areas. In the rat, the mouse and the waltzing-mouse area *z'* is absent.

Sciurus has no cortical areas which are directly comparable with the *z*-areas. Their place is occupied by the areas *t*, *t'* and *t''*. These areas differ from the *z*-areas either by their structure or by their position.

Area *aa* is an area which I could only observe in the rat on the median surface of the hemisphere.

Area *bb* is developed in the mouse, the waltzing-mouse and in *Dipodomys*, *i.e.*, in those animals where the rhinal fissure is absent in the posterior half of the hemisphere. As area *bb* occupies a space which would be traversed by the posterior part of the rhinal fissure, it is probably developed in connection with the absence of this part of the rhinal fissure.

Area *dd* is an area which only belongs to *Dipodomys*.

Dealing with the archicortex, I may say that area *s*, the cornu ammonis, is always present and has the same structure everywhere. It always consists of a layer of pyramids closely crowded together. The transitional area *s'* is also visible in all rodents.

The fascia dentata is always a layer of granules with some scattered stellate cells beneath it. If the granules are inflated ones, as in the mouse, the waltzing-mouse and the guinea-pig, I call the area *r*. If they are non-inflated the area is called *r'* (in the rat, the rabbit, the hare, *Coendu* and *Dipodomys*). *Sciurus* possesses both areas *r* and *r'*.

Finally, I have considered whether some of the nine rodents treated in this paper appear to be more nearly related on account of their cortical areas. Without any doubt this is the case on the one hand with the rabbit and the hare, on the other hand with the rat, the mouse and the waltzing-mouse, *i.e.*, with animals belonging to the same genus. *Sciurus*, *Lepus* and *Mus* show the greatest differences. *Dipodomys* remarkably agrees with *Mus*. *Coendu* more agrees with *Sciurus* and *Mus* than with *Lepus*, but *Cavia* has important points of agreement with either of these three genera. *Sciurus* particularly occupies a special position among the six genera.

Finally, I will compare my results with those of other authors.

I can only do this as to the rabbit, the mouse, the rat and the guinea-pig. No communications about the cortical areas of *Coendu*, *Dipodomys*, the squirrel, the hare and the waltzing-mouse are known to me.

First of all I will discuss the rabbit. The most important researches about the cortical areas of this animal are those of Brodmann (1906 and 1909) and those of Zunino (1909) and Winkler and Potter (1911), which in many respects corroborate the work of Brodmann. It will be most convenient to compare successively the cortical areas, which I found, with the areas which Brodmann

has drawn in the brain-maps of the rabbit, and with the drawings and descriptions of their structure, published by Winkler and Potter.

My areas *a* and *d* do not occur in that shape in the work of Brodmann (1909, Figs. 106 and 107, page 190). Yet, they can be compared very well with the areas 25 and 12. According to me, area 25 (*a*), as well as area 12 (*d*) are running towards the olfactory tubercle; they are not separated from it by a region devoid of cortex. If this homologisation is right, I may conclude that my area *c* agrees with area 32 of Brodmann and *c'* with 24. This is still more probable, because the mutual extent of *c* and *c'* is rather variable in different individuals. So, the position of these areas can be also such as indicated by Brodmann.

Winkler and Potter do not recognise the areas 12 and 25 of Brodmann; at least they do not describe them. Yet, I recognise my area *d* in their drawing II, where it lies above the letters F.Rh and proceeds till the figure 32. In the same way, I recognise my area *a* in Fig. IV of Winkler and Potter, where it is visible to the right of the letters A.l.p. Indeed, here ends the layer, which Winkler and Potter have indicated by small circles. I believe I can recognise my area *a* also in Fig. III.

Winkler and Potter have drawn the areas 32 and 24 in that place, where they are also present according to Brodmann. According to their description in both areas the granular layer is wanting, but an external granular layer, layer II, is present and especially obvious in 32. I called layer III (lamina pyramidalis) the layer which Winkler and Potter call layer II, and took their layer III for the granular layer (layer IV). Indeed, the supra-granular pyramids of this area are inflated in the rabbit. So, they may be confounded with granules, but, bearing in mind the structure of area *c* or *c'* in other rodents, I am sure that my interpretation of the cortical layers is the right one. Winkler and Potter call also in other areas that layer lamina granularis externa, which I consider layer III. This causes some more points of difference.

My area *f* corresponds with the areas 4, 6 and 4 + 6 of Brodmann. It agrees with them according to the drawings in its cortical structure and in its extent on the hemisphere. Brodmann himself remarks that the areas 4 and 6 can only artificially be separated. So, it is evident that they are better joined into a single area *f*. Winkler and Potter too agree in their drawings and description with Brodmann and me.

Area 8 of Brodmann seems to correspond with my area *g*. This is certainly true, when Brodmann has drawn, as if it were externally visible, what in reality lies in the depth of a fissure. Such parts have not been projected by me, because their projection is overlapped by that of other parts. Brodmann, however, draws them in a distorted way. This difference in the way of pro-

jection of the areas will also hereafter appear to be the cause of some apparent differences between Brodmann and me. Yet, area 8 of Brodmann does not accompany the rhinal fissure till its end, as does my area *g*.

Without any doubt my area *g* is not the same area as that which Winkler and Potter (Fig. II) take for Brodmann's area 8. I cannot discover a separate area in this place, not even by means of Winkler and Potter's description. I combine this region with area *f*. On the contrary, I recognise my area *g* also in Fig. II of Winkler and Potter. Here it occupies the bottom of the rhinal fissure and has one limit near the arrow, which indicates the ventral border of Winkler and Potter's area 8, and another limit near the letter F. of F.Rh.

The area 13 to 16 of Brodmann corresponds with my areas *k* and *k'*. I am confirmed in this opinion because Brodmann says that in area 13 to 16 a caudal, granular region (my area *k'*) and an oral, agranular region (my area *k*) are easily distinguished. I was not able to discriminate the two areas into which any of the areas *k* and *k'* can be divided, according to Brodmann. Winkler and Potter always combine the areas 13 to 16 and seem not to discriminate a granular and an agranular region. The different extent of the areas 13 to 16 and *k* and *k'* in the maps of Brodmann and myself may be partly ascribed to the different ways of projection.

Probably Brodmann means by his area 51 the same as I do with my areas *h*, *h'* and *h''*. As *h* and *h''* only differ by the existence of inflated or non-inflated pyramids, and as *h''* does not occur in all rodents, I would eventually approve the combination of *h* and *h''* into a single area 51. Area *h'*, however, decidedly must be considered a separate area, because it is present in all rodents. I conclude from Fig. XVI of Winkler and Potter that they consider my area *h'* a part of area 28. I should divide area 28, as drawn in this figure by a limit, which would run just to the left of the cipher 28. Then, I would call the left part of area 28 area *x* and the right portion area *h'* (compare Winkler and Potter's Fig. XVI with my Fig. 17).

My area *j* probably includes the areas 1 + 3 and 50 of Brodmann. The drawing of area 1 + 3, published by Brodmann on page 103, distinctly demonstrates the high development of the granular layer, which is also a character of my area *j*. Winkler and Potter too have drawn an obvious granular layer in Fig. IV and make mention of it in the text. These authors also seem not to recognise area 50. At least they do not indicate it anywhere.

My area *p* includes not less than the areas 36, 20, 21, 22 and the greater part of area 5 + 7 of Brodmann. I combine that portion of area 5 + 7 which occupies the median border of the hemisphere with 29^d into area *u*. It would be doubtful whether I have not failed in this case to observe structural

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differences which Brodmann was able to see, if my opinion were not supported by the work of Winkler and Potter.

In the first place, they too combine the areas 20, 21 and 22 into one area (20 to 22) and discuss their cortical structure at the same time in Fig. XVI.* Moreover, the arrows, with which Winkler and Potter indicate the limits of the areas 20, 21 and 22 in Fig. XVI, have been drawn in places where to me no change in the structure of the cortex is visible.

Area 36 is indicated as a separate area also by Winkler and Potter. To me it does not differ from the other parts of area *p*.

Winkler and Potter declare in the explanation of Fig. X, that area 7 overlaps area 22 a long way. The differences between the areas 7 and 22, demonstrated by their drawing, as well as those visible in my sections, were insufficient for me to discriminate both areas.

To support my opinion I will point out that also in other rodents I was unable, in spite of much trouble, to divide my area *p* into three or more areas.

Besides, I will point out the dimorphy of area *p*. Perhaps the limit between both types of this area has been taken for the limit between two areas. Yet, as I remarked before, the limit of both types of a dimorphous area is not at all a constant one.

According to me the areas 5, 7 and 5 + 7 of Brodmann are separated into two parts by about the fissure sagittalis lateralis. The median part of these must be combined with area 29^d into area *u*. The lateral portion must be joined to area *p*. This line of demarcation along the fissura sagittalis lateralis has also been observed by Winkler and Potter and has been indicated in Figs. VIII and XIII. They call 5 the area, situated medially of the fissura sagittalis lateralis (and included by me in area *u*); they call 7 the area, situated laterally of this fissure (and included by me in area *p*). So, they accept a line of demarcation between the areas 5 and 7, which runs about perpendicularly to the vague limit, which Brodmann indicates between these areas. It runs, however, quite parallel to the limit indicated by me between the areas *u* and *p*. I will lay greater stress upon this fact than Winkler and Potter do. For I think it very important that Winkler and Potter agree with me in this respect and controvert Brodmann.

As I remarked already, I failed to observe the difference between the areas 5 and 29^d of Winkler and Potter. I combine them into area *u*. Besides, I combine a part of area 18 of Brodmann and Winkler and Potter with area *u*, whereas I join the rest of area 18 to area 17 (my area *w*). Area 18 is not a particularly obvious area. This appears from a remark of Winkler and Potter

* Schuster (1911) also in a recent publication on a monkey (*Papio hamadryas*), does not accept distinct limits between the areas 20-22 of the temporal cortex.

to Fig. XVI, where they say that the areas 17 and 18 can scarcely be separated. In Fig. XVI of Winkler and Potter I should trace the limit between the areas 29^d (*u*) and 17 (*w*) on the bottom of the fissure sagitallis lateralis, i.e., in the middle of area 18.

I am still obliged to remark about area 29^d, that I cannot see its particular structural agreement with the other areas, which Brodmann indicates with 29 and which are indicated by me with *z*. In other rodents too I never got the impression of near structural relations between area *u* and the *z*-areas. For this reason I indicated them with different letters.

Generally speaking, area 17 of Brodmann and Winkler and Potter agrees with my area *w*. Yet, I have drawn the limits of this area somewhat else than Brodmann did, because my ideas about the neighbouring areas are somewhat different. I could not observe the division of the granular layer of area 17 into the layers IV *a* + *b* and IV *c*, as Brodmann (1909) draws in Fig. 76. Indeed, the granular layer of area *w* (17) is particularly broad.

In my opinion area 35 of Brodmann corresponds with my area *y*. I have drawn it in Fig. 17, but I could not indicate its projection in the maps, as Brodmann did, who indicates externally the parts lying in the depth of the fissures. The limits of this area, as they are drawn by Winkler and Potter in Fig. XVI, for instance, do not agree with the limits as I indicate them in Fig. 17. Once more, however, I am able to discriminate in Fig. XVI of Winkler and Potter the areas *y*, *g*, *h* (together 35) and *h'* (28), as indicated by me in Fig. 17. (Compare Fig. XVI and Fig. 17.) If I am right, area *g* has been neglected in this place by Brodmann as well as by Winkler and Potter.

Brodmann's area 28 corresponds with my areas *x* and *x'*, but a portion of my area *h'*, which is not distinguished by Brodmann, has been included by him in area 28. I recognise in Fig. XVI of Winkler and Potter my area *x'*, as it has been indicated in Fig. 17.

Relying on Fig. XVI of Winkler and Potter, I am inclined to believe that area 27^a is my area *s'*. Yet, I also recognise this area in the place where area 29^a passes into the cornu ammonis. This spot has not been indicated by a figure in Fig. XVI. Perhaps also area 26 of Brodmann belongs to my area *s'*. As far as I can see, Winkler and Potter do not mention it.

The areas *r'* and *s* (fascia dentata and cornu ammonis) are not indicated with figures by Brodmann.

Now only the groups of *z*-areas remain to be discussed. It is rather difficult for me to homologise them with Brodmann's areas. Perhaps this can be partly ascribed to the manner of projecting the areas, for this renders these areas especially distorted in the maps.

The areas 23 and 48 of Brodmann are totally absent in my work. Winkler

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and Potter also do not mention area 48, but they observe area 23. I think that Brodmann's area 29^c and a portion of 23 correspond with my area z^{iv} ; area 29^b with another portion of 23 corresponds with my area z'' ; area 29^a combined with area 48 corresponds with my area z'' ; area 29^c corresponds with my area z' , and finally the areas 27^b and 49 correspond with my area z . As to this I must remark that Winkler and Potter indicate in Fig. XIX an area with 29^c, which I should call a portion of area z . One would conclude from their drawings that Brodmann's areas 29^c and 49 (not 27^b and 49) correspond with my area z . But Winkler and Potter do not distinguish area 27^b. Now, in my opinion, they have called area 27^b of Brodmann area 29^c and they have neglected the very area 29^c. Yet, the description which they give of area 29^c does not permit asserting this. I am quite sure, however, that they call my areas z^{iv} , z'' and z'' 29^c, 29^b and 29^a.

Of the other authors who studied the cortical areas of the rabbit, I will first mention Zunino (1909). This pupil of Brodmann generally observed as to the fibre-lamination the same areas which Brodmann had found for the cell-lamination. His work has not helped me in diminishing the differences between Brodmann and myself.

The remarks of Hermanides and Köppen (1903) about the rabbit, the rat and the mouse are of little interest. They distinguish four cortical types, about agreeing with my areas f , w , z' and h . It is somewhat doubtful, perhaps, whether their occipital type is really my area w . They publish in Fig. 10 a well recognisable illustration of area z' , which they call type 3. They call, however, this type 3 (area z') the visual cortex, and homologise it with the area striata (area 17 of Brodmann) of other mammals. Brodmann pointed out this mistake in 1906 already.

Mott (1907) has the same idea as Hermanides and Köppen, and illustrates in his Fig. 4 very well my area z' , which he considers to be the visual cortex.

A very good photograph of area f can be found in van Valkenburg (1911, Plate II, Fig. 7).

The rat is treated by Hermanides and Köppen (1903). They observe in it the same four cortical types as in the rabbit. More important publications about the rat are not known to me.

Our knowledge of the cortical areas of the guinea-pig is already somewhat greater. Mott (1907) describes the area which I call z' , and figures it in Fig. 3. Ernst de Vries (1910) describes the claustrum and figures it with its neighbouring areas in his Figs. 17 and 18.

The mouse, however, is far better known. Ernst de Vries (1910) publishes in Fig. 19 a drawing in which my areas h , k and j are visible. Hermanides and Köppen (1903) deal with the mouse in the same way as they did with the

rabbit and the rat. Their Fig. 8, for instance, does permit recognition of the area which it represents. As area z' is absent in the mouse, they take for the visual cortex what I call area z'' or z''' .

Two very detailed publications about cortical areas in the mouse were issued last year. One of them is the valuable paper of Isenschmid (1911) about the neopallium of the mouse. The other one is the thesis of I. de Vries (1911), where the dorsal and lateral areas of the hemisphere are described and figured.

I am bound to compare carefully my own results with those of Isenschmid and I. de Vries, as they agree in many respects.

Isenschmid as well as I. de Vries obtained results in the mouse, which differ greatly from those of Brodmann. So they could not accept his nomenclature of the cortical areas and were compelled to indicate the cortical areas which they found by a new lettering. In my former publication on this subject (Droogleever Fortuyn, 1911) I did the same. Now, however, I am prepared to accept either Isenschmid's lettering or the nomenclature of I. de Vries in order to avoid confusion. The reason why I prefer to maintain my own lettering is the fact that Isenschmid as well as I. de Vries have only dealt with a part of all the cortical areas of the mouse and not at all with those of other rodents.

Many of the areas of Isenschmid, de Vries and myself can be homologised by means of the descriptions and figures. Yet our brain-maps show considerable differences. This partly is caused by the fact that Isenschmid and I. de Vries have reconstructed mentally their areas. So the projections have become less accurate than mine.

A general difference between Isenschmid, I. de Vries and myself is this, that Isenschmid and de Vries often observe a separate layer II (lamina granularis externa). I was not able to do that, and also de Vries most times speaks about layer II + III. In sections of the brains of waltzing-mice, which were not preserved in formalin, I observed in many areas the superior cells of layer III to be more deeply stained and to be more closely crowded together than the inferior ones. One might consider these cells a separate layer and take it for the lamina granularis externa, as in such preparations all cells are more round than pyramidal shaped. However, in brains of the waltzing-mouse and the mouse, which have been preserved in formalin, this so-called layer II is absent. Moreover, the cells, which lie immediately below the zonal layer, are distinctly pyramidal shaped. From this I conclude that preservation in formalin causes all pyramids to retain their shape more distinctly. For this reason I cannot recognise an external granular layer in the mouse. Also in other rodents, where it is not so troublesome as in the mouse to decide,

whether a layer is composed of granules or of pyramids, I never observed a layer II. So I am inclined to grant more value to my interpretation of the cortical layers in the mouse than to that of Isenschmid or de Vries. Of course, this does not interfere with the homologisation of the cortical areas.

Area *a* of Isenschmid is characterised by particularly large pyramids in layer V. It corresponds with my area *n* and with area C of de Vries, although according to him the largest pyramids of the mouse are to be found in area M and not in this area. Isenschmid publishes a good figure of it in his Fig. 12, and de Vries figures it in Fig. VII. I am glad to be able to refer to the figures of Isenschmid and de Vries, as it was impossible for me to figure all areas of the nine rodents which I studied. I could not detect in my preparations area *a'* of Isenschmid, and I am inclined to include it in my area *n*.

Area *b* of Isenschmid (perhaps combined with the anterior part of area *e*) corresponds with the areas H¹ and H² of de Vries and my area *j*. Isenschmid figures as Fig. 8 a photograph of this area, in which on the right cells and fibres have been added by drawing. This demonstrates the richness in fibres of layer IV. These fibres are the cause of the clouds, which layer IV of this area is showing in my sections, and which are also described by de Vries. Isenschmid, however, does not mention these clouds, which the methylene-blue-stain renders visible. He even says that the fibillary tissue of layer IV is constantly so dense in all areas of the neopallium. I think that the peculiar appearance of layer IV in area *b* ($=j = H^1 + H^2$) has not struck Isenschmid as it did de Vries and myself, because he did not preserve the brains in formalin. I could not see the difference between the areas H¹ and H² of de Vries, and always observed the structure of area H² (compare Figs. IV and X of de Vries).

It is somewhat more troublesome to decide which of my areas correspond with Isenschmid's areas *c* and *d*. Isenschmid himself cannot decide whether area *c* or area *d* is homologous with the area striata (area 17) of Brodmann. Now, without any doubt, area 17 is homologous with my area *w*. For this reason and on account of the figures of the areas *c* and *d*, published by Isenschmid, and on account of their situation in the brain-maps, I infer that area *c* + my area *w* = area striata. Besides, I conclude that area *d* corresponds with my area *u*.

It is obvious that area D of de Vries (Fig. XIV) corresponds with my area *w*, as de Vries himself declares it to be homologous with the area striata. My area *u* seems to correspond chiefly with the areas B' and M of de Vries. Perhaps also area O is included in my area *u*, but to me the description of the areas B', M and O was not clear enough to decide this with certainty.

Area *e* of Isenschmid chiefly corresponds with my area *p*. Area *p*, however, does not extend so far frontally as area *e*. Is it possible that the anterior part of *e*, where Isenschmid observes a greater richness in cells, belongs to area *b* (*j*)? My area *p* corresponds with area I and at least with the anterior portion of area E of de Vries. Both areas I and E belong to the temporal cortex according to de Vries.

Area *f* of Isenschmid must be homologised with area F of de Vries and my area *bb*. This is proved by the figures and its situation in the maps.

I cannot decide which area is meant by area *g* of Isenschmid; it may be a portion of area *t* (my area *z*).

Area *h* is without doubt identical with my area *x*. I quite agree with Isenschmid about its relation to the palaeopallium.

Area *i* of Isenschmid probably corresponds with my areas *k* and *k''*, which I formerly (Droogleever Fortuyn, 1911) combined into a single area. I further believe that area G of de Vries corresponds with my area *k*, and the anterior part of area L with my area *k''*. I could not see the posterior part of area L and I differ from de Vries in the interpretation of the cortical layers of its anterior portion.

I am inclined to believe that area *i'* of Isenschmid corresponds with my area *g*. De Vries has not observed this area.

I feel sure that area *k* of Isenschmid corresponds with area A of de Vries and my area *f*, whereas area *l* of Isenschmid is area B of de Vries or my area *f'*. This is corroborated by the fact that Isenschmid homologises his areas *k* and *l* with Brodmann's area *giganto-pyramidalis* (4 + 6) as I do with my areas *f* and *f'*, and as de Vries does with his area B. I think that his homologisation of area A with area 8 of Brodmann is erroneous.

Area *m* of Isenschmid is identical with my area *c* and area P of de Vries. The cells of this area are all staining uniformly. This was observed by Isenschmid, de Vries and myself. But this affords no reason to accept an external granular layer in this area.

Area *p* of Isenschmid seems to correspond with my area *a''*, although our descriptions diverge.

I cannot recognise an area *o* as it is represented by Isenschmid in his Fig. 11. The fasciola cinerea above the posterior half of the corpus callosum has no definite structure. Above the anterior half of the corpus callosum area *o* would correspond with my area *a'*, but this proceeds ventrally towards the olfactory tubercle and this is certainly not the case with area *o*.

If I am right I combine the areas *n* and *r* of Isenschmid into my area *d*.

Without doubt area 9 of Isenschmid is the same area which I called *z''*. I think de Vries has indicated this area with P'. Area *s* of Isenschmid

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corresponds with my area z'' and area t with my area z . The homologisation of the last three areas is sufficiently proved by the photographs which Isenschmid reproduces of them. Very likely area R of de Vries corresponds with area t of Isenschmid and my area z .

Generally speaking there is a satisfactory agreement in the findings of Isenschmid, de Vries and myself.

THE RELATION OF STRUCTURE AND FUNCTION OF THE AUDITORY AREA (AREA p).

After the general description and comparison of the cortical areas of rodents I wish to find out whether the auditory cortex in different rodents shows anatomical variations which can be brought in connection with its function. In other words, is it possible to find an anatomical character which is more developed as the animal is quicker of hearing and makes more use of it?

This question gives rise to some other questions. Firstly, we have to know what part of the cortex has to be considered auditory cortex, *i.e.*, in what portion of the cortex of the brain are the auditory tracts ending? Further, we must know which animals are quick of hearing, and only then we can find out whether there is a correlation of some character of the auditory cortex with varying degrees of the acuteness of hearing.

I will now describe by what means I have searched for the answer of these questions.

In the existing literature some suppositions have been uttered about the portion of the cortex which would be auditory cortex in rodents. But they are not confirmed by convincing proofs.

Brodmann (1909) gives to a large portion of my area p the figures 20, 21 and 22, which are given in man to the areas of the temporal convolutions. As in man area 22 (the first temporal gyrus) certainly has an auditory function. I suppose that Brodmann would be inclined to attribute also auditory functions to a part of my area p .

Winkler (1907) remarks in his work upon the central course of the nervous octavus in the rabbit, that there are strong arguments in favour of the localisation of the perception of hearing in the temporal part of the cortex of the brain. It is quite natural to consider my area p the temporal cortex. Consequently, also Winkler would judge the perception of hearing to be localised at least in a part of my area p .

Finally, Isenschmid quotes the supposition of Cajal, that the auditory cortex of the mouse would be present laterally of the motor-cortex. Isenschmid presumes that his area e could be meant by Cajal and I identified this area with my area p .

These suppositions are not supported by the decisive proof that area is the auditory cortex. It is not certainly known whether auditory tracts arrive in this area, nor whether total and exclusive extirpation of this area causes degeneration of the corpus geniculatum mediale.

There is still another difficulty of a different nature. One knows that the systems of the cochlear and vestibular nerves are greatly mingled within the brain (compare Winkler, 1907). Now, the question occurs, whether the temporal cortex, area *p*, is only auditory or also equilibratory cortex. Winkler (1907) denies the existence of an area, where the perception of the equilibrium would be localised, as he denies this perception itself. Other authors, however believe the existence of an equilibratory area to be indispensable, or they think that both functions must be attributed to the temporal area.*

It is, therefore, very doubtful what must be considered the auditory cortex in rodents, and indeed, I should have to at once conclude that no answer can be found to the question which was put at the beginning of this chapter. Yet, I will disregard these obstacles for a moment and assume area *p* to be auditory cortex, seeing that there are many arguments in favour of this. Let me try to get an answer now. †

Which rodents are quick of hearing? Physiological experiments upon hearing and even upon the cortical hearing of rodents are unknown to me. So consequently I am unable to answer the question by reference to literature. But, whoever breeds rodents or often observes them gets an impression whether the animal is quick of hearing or not. On account of such observations, chiefly procured from other investigators, I should like to compose the following range of rodents:—

Squirrel.
Guinea-pig.
Rat.
Mouse.
Rabbit.
Waltzing-mouse.

The first of these animals, the squirrel, is the quickest of hearing, the last one, the waltzing-mouse, is absolutely deaf.

One can expect that an animal with many cells of Corti in its auditory organ has the auditory function better developed than an animal with few

* I do not think that this opinion can be supported by the fact that area *p* is often dimorphous. If *p* were the only area which could be dimorphous, one could look upon this as an area with a double function and a double structure. Now, this can hardly be done.

† Assuming area *p* to be auditory cortex as well as equilibratory cortex, I am quite unable to study the relation of its structure and function.

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cells of Corti.* Previously, I thought that it was not improbable that an animal with many cochlear-windings, and consequently with a relatively long cochlea, would possess many cells of Corti, and consequently a well-developed hearing. (This holds also true, when not the cells of Corti but the membrana basilaris, or the free endings of the cochlear nerve-fibres, are the recipients of the auditory impressions.) So I counted the number of cochlear-windings in all my rodents and found the following numbers, some of which are agreeing with those of Gray (1908) :—

Number of cochlear-windings :—

Guinea-pig	3½
Dipodomys	3¼
Squirrel	2¾
Hare	2½
Rabbit	2½
Rat	2¼
Coendu	2¼
Mouse	2
Waltzing-mouse	2

Yet, one has a better means albeit a much more laborious one, to estimate the number of cells of Corti in the cochlea, *i.e.*, to count the number of nerve-fibres of the cochlear nerve. Moreover, one might expect that the relative number of these fibres would be an indication of the number of ganglion-cells of the auditory cortex. So I approximately counted the number of cochlear nerve-fibres in the way described in the chapter on material and methods. I found approximately the following round numbers :—

Number of cochlear nerve-fibres :—

Coendu	18,000
Rabbit	15,000
Hare	10,000
Squirrel	10,000
Guinea-pig	7,000
Rat	3,000
Mouse	2,000
Dipodomys	1,700
Waltzing-mouse	400

* For the moment I suppose that the cochlear nerve exclusively transmits impressions of hearing, Winkler (1907) thinks that the cochlear and vestibular nerves are both in the service of the hearing and the equilibrium.

Although these numbers can be more precisely defined, they demonstrate how much the number of cochlear nerve-fibres diverges.

Moreover, the number of cochlear-windings appears to be not at all proportional to the number of cochlear nerve-fibres.

Besides, I did not get the impression (compare the first table with the third) that indeed the animal which has the largest number of cochlear nerve-fibres is the quickest of hearing. On the contrary, this number seems to be more nearly (although not exactly) correlated with the size of the body or rather of the brain. Compare for this statement the third table with the next two :—

Size of the body—	Size of the brain—
Coendu.	Coendu.
Hare.	Hare.
Rabbit.	Rabbit.
Guinea-pig.	Squirrel.
Rat.	Guinea-pig.
Squirrel	Rat.
Mouse.	Dipodomys.
Waltzing-mouse.	Mouse.
	Waltzing-mouse.

Consequently, also in an indirect way I was not able to decide which rodents are quick of hearing and which are not. Moreover, if indeed the development of the auditory cortex were nearly correlated with the number of cochlear nerve-fibres, one ought to observe more differences in the structure of area *p*, than one actually does (compare Plate II). The number of cochlear nerve-fibres in the mouse is nine times less than in Coendu, but none of the layers of area *p* varies so greatly in its development. Also the relative size of area *p* did not seem to be correlated with the auditory function.

In this situation I could do nothing but to observe whether the result of Mott would be demonstrable in the auditory cortex per analogiam.

According to this result the layer of supra-granular pyramids would be more developed as the function of the cortical area was more developed.

So I calculated in all rodents the relation of the breadth of layer III to the total breadth of the cortex in area *p*. If one desires to calculate exactly this relation, one ought to measure the breadth of the cortex in numerous spots as it is rather variable. I obtained by a small number of measurements the following numbers. They give quite a new arrangement of the rodents, differing from those of the preceding tables.

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Relation of the breadth of layer III to the total breadth of the cortex :—

Rabbit	0·29
Guinea-pig	0·27
Rat	0·26
Hare	0·25
Coendu	0·23
Squirrel	0·22
Dipodomys	0·20
Mouse	0·19
Waltzing-mouse	0·18

Finally, I have more exactly compared the mouse and the waltzing-mouse, because they are two animals which chiefly differ by their auditory function and not by the size of the brain or of area *p*. Indeed, the mouse is rather quick of hearing but the waltzing-mouse is deaf, and if ever we might expect here, that the functional difference would be also anatomically visible in the cortex of the brain. Yet, this is not the case. A superficial contemplation of the cortex of area *p* does not offer constant differences between the mouse and the waltzing-mouse. But I also took pains to measure the breadth of layer III and to calculate exactly the number of supra-granular pyramids in a mill.³ I obtained the following averages of 10 observations in each animal ; the numbers have been rounded off :—

Breadth of layer III, area *p*.

Mouse 0.17, 0.18, 0.18 mill.

Waltzing-mouse 0.13, 0.16, 0.18, 0.19, 0.17 „

Number of supra-granular pyramids per mill.³

Mouse 244,000, 214,000, 271,000.

Waltzing-mouse 280,000, 217,000, 227,000, 217,000, 213,000.

Generally speaking, the waltzing-mouse has a somewhat narrower layer of supra-granular pyramids in area *p* than the mouse has, and the cellular density of this layer is less. Yet, the numbers vary transgressively, and further observations perhaps would have reduced this difference. This result is not contrary to what might be expected on account of the results of Mott. But, it is of little importance, and I dare not positively state that the waltzing-mouse has a poorer development of the supra-granular pyramids in area *p* than the mouse. It remains very well possible to confirm also for the auditory cortex the results of Mott, when animals belonging to different orders are compared, as Mott did. To a certain extent this is made probable by a fact which I could verify myself, viz., that in man the supra-granular pyramids of the auditory cortex are better developed than in rodents.

I did not observe any reduction of layer III with increasing age of the waltzing-mouse. Yet this might be expected, as, according to van Lennep (1910), the auditory organ begins to degenerate after birth and before this the cortex of the brain has no cause to degenerate itself. The last number of those published above for the waltzing-mouse refers to a mouse aged two months; the last number but one refers to a mouse aged three months; the remaining numbers refer to full-grown waltzing-mice. The last two numbers do not deviate from the other ones in a definite direction.

I was not urged by the preceding results on undertaking measurements and calculations as to other layers of area *p*.

Inadequate knowledge of functional capacity of the various rodents examined as regards hearing do not permit an answer to the questions propounded, but this much I am able to state.

I cannot find in area *p*, the auditory cortex (?) of rodents, any variations which could be correlated with function. Neither can I pretend, however, that such variations do not occur.

CONCLUSIONS.

I will now summarise the principal results of my investigations. Firstly I can say that the cell lamination and the situation of the areas in the cortex of the brain generally agreed in different rodents, although important differences occurred.

Some areas (*f*, *j*, *p*, *w*, *x*, &c.) were present in all rodents which I studied. Other areas appeared to be characteristic for some genus (for instance, area *a*" for the genus *Mus*), or they were wanting in some genus (for instance, area *n* in the genus *Lepus*). Still other areas appeared to characterise some species (for instance, area *aa* of *Mus decumanus*).

Animals belonging to the same genus generally more agreed than animals belonging to different genera. This might be expected, of course.

In some rodents some areas (for instance, *f*, *j*, *p*) demonstrated a not uniform structure. In such areas two types of cell lamination, different from one another in some respects, were irregularly mixed. I called such areas dimorphous areas. As far as I know, this phenomenon has not been described by other authors.

The cells of the lamina pyramidalis and the lamina ganglionaris (layers III and V) may be either distinctly pyramidal-shaped or they may be more rounded and pale-tinted. In the first case I called them typical pyramids in the latter case inflated pyramids. There are cortical areas, where the

pyramidal cells are all either typical or inflated ones. In other areas, however, they are for some unknown cause sometimes inflated and sometimes typical pyramids. In consequence of this such areas have a very variable appearance.

In many cases I only detected the presence or the structure of an area in some rodent after I had seen it in other rodents. So, for instance, area *a'* of *Sciurus* has been elucidated to me by *a'* of *Mus decumanus*; area *b* of *Coendu* by *b* of *Sciurus*; area *h'* of the mouse by *h'* of the rabbit; area *k''* of the mouse by *k''* of *Dipodomys*. Thus, it appears that in studying the cortical areas of an animal the comparative anatomy can render useful services.

The areas *a*, *b* and *c*; *e*, *f* and *f'* and also *h*, *h'* and *x* showed remarkable structural transitions. For their description I refer to pages 234, 333 and 334.

Probably area *p* has to be considered auditory cortex, although the convincing proof of this could not be given by comparative anatomical researches.

No variation in the development of this area connected with its supposed function could be demonstrated. Partly this was due to the impossibility to decide which rodents are quick of hearing and which are not. The direct statements about this were not corroborated by the indirect ones. The number of cochlear-windings appeared not to be correlated with the number of cochlear nerve-fibres. The latter in its turn appeared not to be correlated with the development of the auditory function, but rather with the size of the brain. There was no apparent correlation between the development of some part of the auditory cortex and the number of cochlear nerve-fibres. The relation of the breadth of the layer of supra-granular pyramids to the total breadth of the cortex seemed to be not connected with the development of associative hearing, as I expected on account of the results of Mott.

The average of the breadth of layer III in area *p* and of the cellular density in this layer were somewhat less in the waltzing-mouse than in the mouse. The obtained values varied transgressively.

No changes in area *p*, which were correlated with the age of the animal, could be found.

PLATE I.



Fig. 1. *Sciurus vulgaris*. Area b.



Fig. 2. *Lepus cuniculus*. Area x.

PLATE II.



Fig. 1.

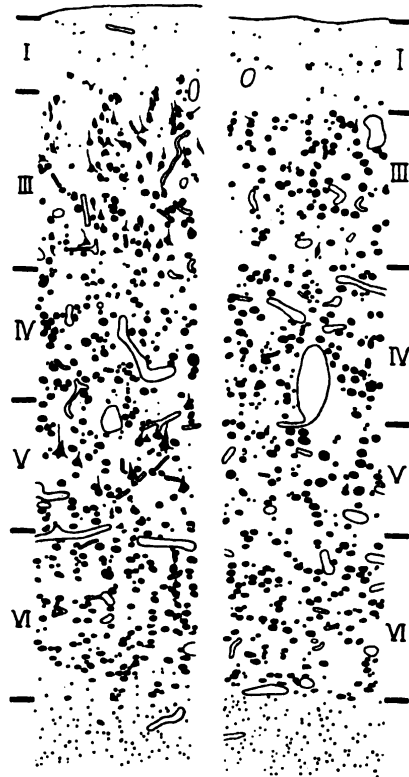


Fig. 6 *Cavia cobaya*.

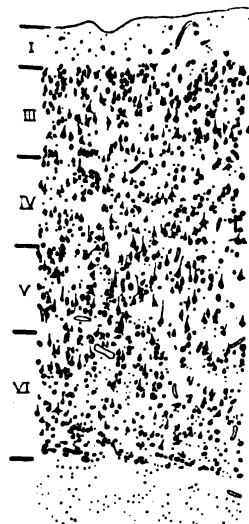


Fig. 9. *Dipodomys merriami*
nitratoides.



Fig. 7. *Coendu prehensilis*.

LIST OF ABBREVIATIONS.

In all figures the cortical areas have been indicated with the letters *a, a', a'', a''', b, c, c', &c.*

A region free from cortex is indicated with *o*.

The dotted lines in the brain-maps indicate the limits of the areas.

The '—' line in the brain-maps indicates the region where the hemisphere is united with the other parts of the brain.

In all figures means:—

B.O.	=	Olfactory bulb.
C.A.	=	Anterior commissure.
C.C.	=	Corpus callosum.
CL.	=	Clastrum.
F.C.	=	Fissura cinguli.
F.R.	=	Rhinal fissure.
F.S.L.	=	Fissura sagittalis lateralis.
S.	=	Tractus olfactorius.
T.O.	=	Olfactory tubercle.
V.	=	Ventriculus.
II.	=	Optical nerve.
I.	=	Zonal layer (lamina zonalis).
III.	=	Layer of supra-granular pyramids (lamina pyramidalis).
IV.	=	Granular layer (lamina granularis interna).
V.	=	Layer of infra-granular pyramids (lamina ganglionaris).
VI.	=	Polymorphous layer (lamina multiformis).
III ^a , III ^b	=	Layers, into which layer III is divided.
VI ^a , VI ^b	=	Layers, into which layer VI is divided.

PLATE I.

FIG. 1.—*Sciurus vulgaris*. Area *b*. Camera lucida drawing. 115 mag. Layer III is absent. Layer IV consists of inflated granules.

FIG. 2.—*Lepus cuniculus*. Area *x*. Camera lucida drawing. 115 mag. Layer III is divided into III^a and III^b. Layer IV is poor in cells and is obvious as a light band. Layer V is absent.

PLATE II.

FIGS. 1-7.—Area *p*. Camera lucida drawings. 67 mag.

FIG. 1.—*Sciurus vulgaris*. Layer IV is dimorphous; to the left inflated granules.

FIG. 2.—*Lepus cuniculus*. The layers III and V are dimorphous; to the right inflated pyramids.

FIG. 3.—*Mus decumanus*.

FIG. 4.—*Mus musculus* (compare Fig. 8).

FIG. 5.—*Cavia cobaya*. Dimorphy. To the right inflated pyramids in the layers III and V; to the left typical pyramids.

FIG. 6.—*Lepus europæus*.

FIG. 7.—*Coendu prehensilis*.

FIG. 8.—*Mus musculus*. Area *p*. Camera lucida drawing. 115 mag. (Fig. 4 more enlarged.)

FIG. 9.—*Dipodomys merriami nitratoideus*. Area *p*. Camera lucida drawing. 67 mag.

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The Relation of Head Injury to Nervous and Mental Disease.*

By F. W. MOTT, M.D., F.R.S., F.R.C.P.,

Physician to Charing Cross Hospital; Pathologist to the London County Asylums.

THE medico-legal importance of distinguishing cause from coincidence in cases of head injury in relation to nervous and mental disease has come into increased prominence since the introduction of the Workmen's Compensation Act; and when the State Insurance Bill becomes law the diagnosis and prognosis of neuroses and psychoses following trauma, and the detection of fraud and malingering, especially in cases of slight head injuries in which obvious and visible signs are absent, will be a constant source of anxiety to members of the profession.

Employers, except in the case of corporations and large companies, as a rule insure against accident or injury to their employees; the result is that workmen and employees are more certain of obtaining adequate compensation for injuries received; for should a company dispute the claim and the case come before a jury, just as is the case when railway, bus, tramway or other companies or corporations carrying the public are defendants in actions for damages, sympathy is generally, and sometimes not properly, felt for the individual rather than for the corporation or company. The knowledge of this fact has led to improper claims being made, and the insurance companies, like the railway companies, have frequently been compelled to resist the payment of unjust claims. Unfortunately this has led to just claims sometimes being classed as exorbitant, causing legal intervention, lawsuits, and much money being thereby frittered away in costs, to the benefit of neither party. If the medical men interested would act in the same spirit as when they are called upon to decide in a consultation what is the nature of a man's disease, what is the outlook, and how best to treat his condition, how much better it would be. Would they in their senses recommend the worry and anxiety of a lawsuit to a man suffering from traumatic neurosis or psychosis? The assessment of damages must in the great majority of cases depend upon the medical evidence, and

* Opening of a discussion at the Neurological Section of the British Medical Association held at Birmingham, August, 1911.

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it would be better if the medical men employed respectively by the injured person and the company would banish from their minds all question of damages until they had agreed upon a joint report regarding the nature of the injury, the disease caused by it, the prospect of complete or partial recovery, the temporary or permanent incapacity for employment, the liability to late after-effects or shortening of life, and other questions which might arise were they called upon to give evidence in a court of law. Should they not agree upon any or all of the points, then before resorting to legal intervention it would be better to agree to settle by arbitration, an expert of recognised ability and integrity being called upon to decide upon the points of variance, his opinion being regarded as final by both parties. These points having being settled, an actuary can calculate the claims more justly than a jury.

Such a mode of procedure would greatly benefit all genuine and deserving claims; now, unfortunately, legal intervention often leads to deserving cases being subjected to prolonged worry, anxiety, sleeplessness, and consequently bodily ill-health. A pending lawsuit to recover a just claim by a sensitive and nervous person suffering from traumatic neurasthenia will aggravate the symptoms and lead to their prolonged instalment. As an example of this I will relate a case that occurred in my practice.

I was asked to see a case in consultation with the medical adviser of a bus company. A carman, a steady man who had not been away from his employment for thirty years, had received injuries and shock in consequence of the motor bus colliding with a cart and throwing him violently to the ground. He received a severe shock, but was able to get up, although unable to return to his work; he lay in bed and was visited by his own doctor, who took a somewhat grave view of his case; the effect of this probably was to suggest to the man that he might become paralysed, and the fear of such a condition, together with legal intervention and a possible lawsuit, had led, when I saw him, to sleeplessness, general bodily ill-health, and muscular wasting. Although I could find no obvious evidence of nervous disease, yet I felt at once the man was not malingering but was suffering from the causes I have mentioned, and was physically unfit for his employment. I ascertained that the company had no intention of resisting the claims by going into court. I advised them therefore to do their best to get the man well, and offer to send him to a convalescent home for three months, and to assure him that if he did not recover completely they would provide for him until he was able to return to his work.

Medico-legal cases naturally fall into two great groups—(a) functional,

(b) organic. It is with the former, where the symptoms are almost if not entirely subjective, that the greatest difficulties to the medical man arise, but in many organic diseases following head injury, as I shall show by actual cases, great difference of opinion may arise as regards responsibility and assessment of damages. Likewise, medical opinion may differ as to how far the resulting head injury was a prime cause, a co-efficient, a contributory cause, or a mere coincident of the symptoms for which damages are claimed. Cases admitted to the general hospitals on account of head injury are usually obvious, and have severe symptoms which clear up frequently without any operative influence. What becomes of a large number of these cases admitted to hospitals in London, with its wide area of shifting population, we do not adequately know. What, however, has astonished me is the relatively few cases that afterwards come into the asylums. There are a great number of people every year who receive very severe head injuries, and a considerable number of them require operative treatment, yet comparatively few of these come into the London asylums.

Of sixty-five cases of fracture or concussion admitted to Charing Cross Hospital within the last few years 22 per cent. died. The remaining 78 per cent. left the hospital; in some cases they were sent to the infirmary, in other cases to their homes or convalescent hospitals. Mr. Fenwick wrote to the addresses of all the cases that left the hospital, but only obtained answers from thirteen. A brief summary of these thirteen cases is given. One of the thirteen cases was afterwards admitted to Horton Asylum; he was certified and re-certified as suffering with "traumatic insanity." This patient was admitted to Charing Cross Hospital suffering with fracture of the base—extra-dural and subdural hæmorrhage; two operations were performed. He was afterwards discharged to Camberwell Infirmary certified as suffering from traumatic insanity, and sent to Horton Asylum three months after the accident. The notes on admission state: He is the subject of mania. He is a little confused and rambling in conversation, with an abnormal sense of well-being and lack of realisation of his position. His wife stated that he used to have occasional drinking bouts, and during them he became very suspicious and threatening towards her, and she went in danger of her life. His occupation was that of carpenter to an organ builder. He is still in the asylum, four years after admission, and has been certified several times as a case of "traumatic insanity." A year ago his daughter was admitted to the asylum suffering from "volitional insanity." The history given prior to the accident, together with the fact that the daughter has become insane during adoles-

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cence, supports the contention that there were two factors at work—an inborn temperamental, the more important, and an exciting factor, “the head injury,” combined with drink. The following case, reported by Dr. Robert Jones in vol. iii, ‘Archives of Neurology,’ is of considerable interest :

CASE 1.—Male, aged 26 years, single. Admitted to asylum from prison. Up to the age of twenty-one he was an abstainer and held a responsible position. He met with a serious accident, falling a distance of over 40 ft. down a lift, through the bursting of a hydraulic cylinder. He was picked up unconscious and remained so for several days, having fractured his skull and sustained a severe injury to the right frontal lobe, some of the brain substance having escaped through the wound. He remained in hospital for about two months, and four months later attended St. Bartholomew’s Hospital, where portions of dead bone were removed from the wound. He was under treatment intermittently for about two years, and when sufficiently well was given some light work to do, but he was found to be of no use, and eventually—about two and a half years after the accident—he was pensioned. Up to the time of the accident he was bright, active, energetic, and trustworthy. He was a life abstainer and a Sunday school teacher. He was apparently forging his way to the front—gaining the respect of his employers and giving general satisfaction. After the accident, however, there is a record of gradually increasing moral obliquity and mental infirmity. During this period he has been three times convicted of indecent behaviour; on the first occasion (two and a half years after the accident) he was fined; on the second he was bound over, and on the last occasion he was found guilty but insane, and was sentenced to be detained during His Majesty’s pleasure. Condition on admission to asylum: Viscera normal. Reflexes normal. Sensibility unimpaired. Pupils equal and react to light and accommodation. No affection of the ocular muscles. He complained that his sight had become impaired for long distances since the accident. There was an irregularly depressed linear scar, 6 cm. long, vertically across the forehead. It was about 5 cm. to the right of the middle line and extended upwards through the right side of the bridge of the nose, being 5 cm. in depth in the deepest place. The right frontal bone was obviously depressed and the skin was scarred above it. His mental state was that of organic dementia secondary to injury of the brain. His memory was greatly impaired. He was irritable, excitable, and preferred solitude, as society worried him. He further admitted that his home and those previously dear to him had lost their attraction for him.

He had the delusion that people in the streets spoke of him, that they made signs and annoyed him by talking over his affairs, and he felt himself watched. He did not appear to realise his position, and talked freely and shamelessly. It is of interest to note that there was no family history of insanity in this case.

Traumatic epilepsy may be the result, and a few cases may be found in the asylums of men with trephine holes, and I have met with one case of fracture of the base which led to chronic basic meningitis and internal hydrocephalus. This case is of sufficient interest to refer to in a little detail. It supports the statement of Köppen that a post-traumatic dementia may occasionally occur which may be mistaken for general paralysis.

CASE 2.—Male, aged 47 years, shipwright, was admitted to Poplar Hospital four years previous to admission to Claybury (June, 1897) suffering from a fracture of the skull. He was a temperate man, and prior to the accident nothing ailed him. His wife stated that the symptoms came on after the accident two years previously—"he was wandering about the house looking for money." She had been married nineteen years: three miscarriages, one child lived nine months, no children living.

State on admission.—There is an old depressed linear scar of the vertex. There was a history of syphilis and gonorrhœa. The pupils were equal, reacted to light and to accommodation. The gait was steady, co-ordination of hands good, but a coarse tremor was present. The hearing was very defective; he could only hear the tick of the watch a few inches from the ear. He is suffering from dementia; states that he was in this building ten years ago. He has aural hallucinations and some loss of memory. He does not know where he lives; he is confused and cannot give a connected account of himself. He denies that he has been drinking much lately. States that he gets fidgety, but not very excited or depressed. Several medical officers of experience, including Dr. Jones, regarded him as a general paralytic in the notes that follow.

July, 1897: Dr. Jones's note is as follows: He is suffering from dementia paralytica (traumatic?). He is confused and lost in his statements, rambles, and repeats himself. His memory is impaired, and he has no correct knowledge of time or place. He thinks that he has been here a month, and that this is Maryland Point. His speech is hesitating, and he has a drawl suspicious of general paralysis. His appearance is dull, vacant, and listless. Talks of being smashed to pieces in a shipyard. (This was true.) In fair nutrition but impaired health. His pupils barely

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react. His knee-jerks are active. His gait is ataxic. He has large scalp scars and several on his knees and arms. His tongue quivers somewhat, and he is sallow. Then follows note in red ink: Pupils equal and regular; react to light and to accommodation. Vision: R. $\frac{6}{6}$, L. $\frac{6}{6}$. Cornea, lens, and fundus normal in each eye.

After this date the notes are such as usually occur in a case that is regarded as a general paralytic, and he died eighteen months after admis-

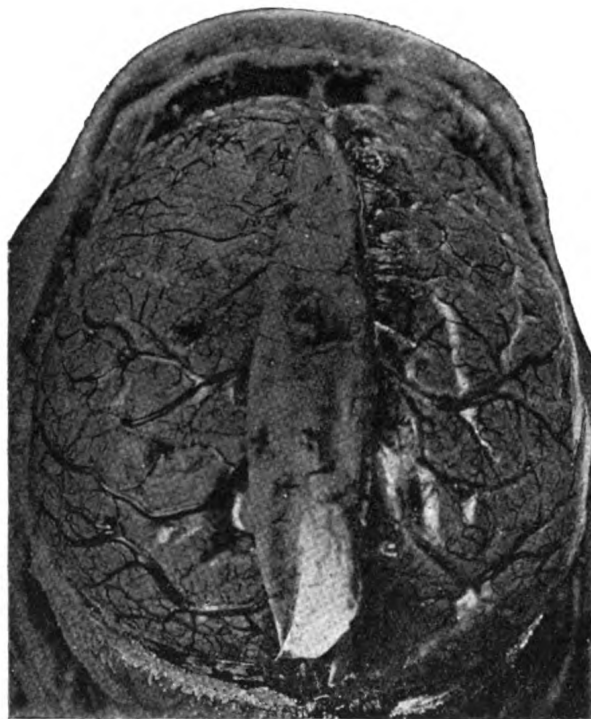


FIG. 1. —The brain exposed after removal of the calvaria and reflection of the dura mater to middle line.

sion. It may be remarked, however, that Dr. Wollesley Lewis (January 15th, 1898), stated that this was not like a case of general paralysis. The patient died of broncho-pneumonia. At the *post-mortem* examination old basic meningitis, caries of the left petrous bone, and blocking of the channels connecting the ventricles with the subarachnoid space were found. The aqueduct of Sylvius was greatly distended, and there was marked internal hydrocephalus of the lateral and third ventricles, causing marked flattening of convolutions, which were dry and sticky-looking (see Fig. 1). This must have led to the marked increase of intra-cranial pressure

causing double optic neuritis. This was discovered at the necropsy when the backs of the eyes were removed.

Again, a small proportion of general paralytics are admitted with a history of head injury which took them to the infirmary or hospital.

From a medico-legal point of view the interest does not lie so much with cases of head injuries causing (a) fracture, (b) hæmorrhage, (c) localised meningo-encephalitis, resulting in organic brain disease, because

*finder the doctors charge when we had
finished coaling ship we had to take down
all the gear that we lent to the Colliers
as the only thing is lent to us is the four steam
whistles we draw the coal out of the Colliers
Hells, and the Mariner, Seaman and Stokers
lift the bags into a shoot and when they
are all filled up with coal we take all the gear
that belongs to the Renown, three or four Seaman
were taking the pin out of a shackle when
the pin was taken out there was no warning
to lay hold of it so it fell on to the steam Valve
and the spindle breaking off struck me on
the left forehead and made a nice cut. ^{there}
^{love you} were only saying in one of your
letters about 3 weeks don't you have any
accident but I had to get that knock on the
head*

FIG. 2.

there are definite signs and symptoms of the actual injury; and there is paralysis or other resulting loss of function about which there can be no dispute as to its being the prime, and often, indeed, the sole causal factor. It is quite possible, however, for a severe head injury even necessitating trephining to occur, and yet this may only be a coincidence or the exciting factor.

CASE 3.—Male, aged 35 years. Was admitted to Bexley Asylum, October 28th, 1903; died April 20th, 1907. The patient had been an engineer's artificer in the Royal Navy. He was on the "Renown," stationed

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in the Mediterranean. He wrote frequently to his wife, and these letters were very affectionately worded, and denoted love for his home, his wife, and children; they showed no sign of failing intelligence or loss of the auto-critical faculty. In August he met with an accident, which is described in a portion of a letter to his wife, here reproduced (Fig. 2). A month later he wrote, addressing his wife as Lady R—, and in October—two months after the accident, as the letter shows—there are marked grandiose delusions of wealth, and the handwriting has markedly deteriorated (Fig. 3). The comparison of these two letters shows that immediately following the accident the degenerative process, if it were present, did not manifest itself in his letter to his wife describing the

"and I am benighted. I have 10,000,000,000
I am pleased to know that Uncle is
is going to get me a situation
and also you I have sent
by 1,000,000,000,000
I am pleased to say that

FIG. 3.

accident; within two months there were very marked signs of dementia, indicative of a degenerative process. Some time after admission to Bexley Dr. Stansfield trephined over the frontal eminence, and it was found that the membranes were adherent at the seat of the injury. He did not benefit much by the operation. He became gradually more demented, and died three years and three months after the accident. The anatomical signs of general paralysis were found well marked *post-mortem*. The man may have previously suffered from syphilis, and to those who believe general paralysis always to be due to syphilis the head injury only acted as the determining factor. Still, it may be reasonably asserted that if this man had not met with the accident he would not have suffered from general paralysis; or, at least, the chances were 50 to 1 against it occurring, for only about 2 per cent. of the subjects of syphilis subsequently develop

general paralysis. Now, there are several facts in this case which support this contention. First, the man was in good health, employed as a skilled artisan: secondly, the injury was the result of an accident in no way dependent upon the man's actions or state of consciousness; thirdly, letters prior to and immediately after the accident were not indicative of any mental decay; fourthly, there was a definite correlation of the accident with the onset shortly after of mania; fifthly, the patient lived more than three years after the onset.

There is only one point which might be considered against the view that the accident was the determining cause in Case 3, namely, the patient may have been in the paralytic stage when the accident occurred; the only tittle of evidence in favour of this was the fact that he began his letters to his wife in an effusively affectionate manner, but then the wife said that there was no difference in his letters to those she had always received. This interesting case is the most conclusive one I have met with of injury causing general paralysis. The wife unsuccessfully endeavoured to obtain some compensation from the Admiralty, and Dr. Stansfield, to whom I am indebted for the notes of this case, wrote to the Admiralty expressing the decided opinion that the accident was the cause of the mental disease.

It would be difficult to convince a jury that a head injury sufficiently severe to necessitate such a serious operation as trephining was not the prime cause of general paralysis, insanity, or epilepsy, and the fact that there was a history of acquired syphilis in the first mentioned and a neuropathic history in the last-named would not convince the jury that if this head injury had not occurred the patient would have suffered from any of these conditions. But is it not logical to assume that a man may sometimes suffer as seriously from "*commotio cerebri*" as from a fractured skull? There may be little or no external evidence of injury to the head, nor may there be any gross nervous trouble—for example, irritation or paralytic phenomena—but the higher functions of the brain as an organ of mind have been profoundly disturbed, for the man may have lost consciousness for some time; as a rule he is unable to recollect how the accident happened or the experiences of his life for some time, perhaps hours previously; and here I may remark we can differentiate between memory and recollection. Memory is the storing away of perceptor experiences out of consciousness, and recollection is reviving by will and association the images of those experiences in consciousness. Some of these patients, after they have recovered

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from the shock and are convalescent, are able to revive in consciousness the events which happened. The great feature of "commotio cerebri" is the resulting inability of the brain to exercise sustained attention on account of the mental fatigue which occurs. There is a disturbance of the physiological activities of the nervous elements which form the anatomical basis of consciousness. But this seat of consciousness and the higher function of the brain is the cortex cerebri, the structure latest developed.

COMMOTIO CEREBRI: ITS EFFECTS ON MEMORY.

Now, it is a fact that trauma, accompanied by horrifying circumstances, causing profound emotional shock and terror, has a much more intense effect on the mind than the simple head injury would cause, in spite of the fact that for some time after the injured subject may be unable to recall the circumstances. There is such a thing as "psychical trauma," and accepting this we can understand how it is that a drunken man receiving a head injury under such terrifying conditions as to cause mental shock suffers less than a man who is fully conscious. A nervous breakdown may result from psychical trauma alone, and the only explanation of this which I can offer is that the whole nervous system is in a state of bio-rhythm in response to stimuli entering all the sensory avenues which arouse in consciousness feelings and thoughts by association with past experiences stored in the memory. Physical or psychical trauma, still more the two combined, destroy for a time this vital reaction of the neurons.

Relatively only a few of the association memories cross the threshold of consciousness, and those that do become vivid by attention. It is attention that uses up nerve energy of the innumerable neurons that exist in the cortex; it may be premised that the commotion of the brain either biophysically or bio-chemically interferes with the functions of the neurons which form the anatomical substratum of consciousness. But it may be asked why is it that the memory images of earlier experiences can be recollected, whereas those which happened just before and after the accident cannot? The following explanation may be offered: A present experience involves a conscious perception and attention, with transformation of potential into kinetic nerve energy; it may be likened to the chemical change produced in a sensitive photographic plate. The next perception involving conscious attention requires a new sensitive plate:

in the meanwhile the last perception has faded out of consciousness, and is undergoing a process of fixation. There is thus a series of perceptions constituting successive experiences, which are linked together by associations in time and place. But all perceptions are dependent physically upon different modes of motion in complex and varied combinations, and the molecules of the neurons are correspondingly set in motion. There is no reason to suppose they (the molecules) come to rest immediately after the external stimulus is changed; it is quite possible that the molecular movements resulting from a particular external stimulus continue long after the stimulus has ceased to act, by reason of the fact that the association neurons which have previously been affected by a similar molecular rhythm are set in vibration, and reverberation after reverberation occurs subconsciously long after the primary perceptor effect of consciousness has passed away. A successive series of experiences are thus linked up and intimately interwoven by conscious and subconscious cerebration. A sudden commotion not only breaks one or more of the series of perceptor links, but throws out of gear the mechanism of association in time and place that integrates and co-ordinates the succession of experiences of the conscious self upon which memory and recollection depends.

Consequently events that happened just previous to the accident, although conscious and perceived at the time, cannot be recollected. In alcoholic psychosis the same thing happens. Conscious perception of each link in a chain of events occurs, but they cannot be stored away out of consciousness to be recollected because, owing to the effect of the poison, the process of fixation, first by attention and afterwards by subconscious bio-rhythmical reverberation of the association neurons, cannot take place.

Again, a further proof that *commotio cerebri* produces a profound disturbance in the functions of the cortical neurons is afforded by the well-known fact that a man who has suffered with a severe head injury is rendered intolerant of alcohol; a dose which previously had little or no effect, after head injury readily produces toxic symptoms.

DIAGNOSIS OF FUNCTIONAL NEUROSES AND PSYCHOSES.

The diagnosis of functional neuroses or psychoses and the detection of malingering is always a source of much tribulation to medical men. To form a just opinion on a case requires the exercise of a sound judgment of character and knowledge of the previous conduct and habits of the injured

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person, in order to estimate the effects of a head injury in which all the symptoms are of a subjective character.

Again, the medical man who knows, or has ascertained, that the patient is the member of a stock in which epilepsy, insanity, hysteria, or other neurosis or psychosis occurs among its members, will recognise the probability of a neuropathic tendency; if there is not actually potential epilepsy or insanity in his patient, he will infer that a comparatively slight trauma in such an individual, such as that produced by a blow on the head which may or may not cause loss of consciousness, without any fracture or obvious injury of the head, is quite sufficient to cause serious symptoms in an individual predisposed to a neurosis or psychosis by an acquired or inherited *locus minoris resistentiæ* in the nervous system. Thus a man who is known to be a chronic inebriate, or a subject of lead-poisoning, or a person who has had syphilis, especially one who by his habits of life has been known to have exhausted his nervous system by sexual excesses, mental stress involved in gambling and speculating, associated with smoking and drinking, restless by day and sleepless by night—if such an individual on the verge of neurasthenia receives a slight injury a question of compensation may arise. A certificate may be written to the effect that he is suffering from “traumatic neurasthenia,” thus implying that the injury was the sole cause of his condition, and a claim for compensation made.

Again, as the result of head injury to a chronic inebriate, “delirium tremens” is not an infrequent consequence, and this for the sake of compensation claims has been termed “traumatic neurasthenia.” Indeed, so much fraud has been perpetrated under the term “traumatic neurasthenia,” that many lawyers know that such a diagnosis does not carry much weight in a court of law unless the man’s previous character and conduct are above suspicion. The medical experts employed by railway companies are fully aware that after a settlement has been effected the symptoms frequently rapidly disappear, but it does not always follow that because a rapid improvement has taken place after the claims have been settled the symptoms of neurasthenia following head injury have not been genuine. Many patients relieved of the anxiety and sleeplessness accompanied by bodily ill-health caused by the pending lawsuit soon recover, because an important cause of the exaggeration and prolongation of the nervous exhaustion was thereby removed.

The differential diagnosis of traumatic neurasthenia from malingering is not an easy one, and it is of great importance, because a man may truly

be incapacitated, especially in occupations involving mental work, for a considerable time after the injury. Seeing that the symptoms may be all subjective, it may be extremely difficult to decide how far the symptoms are genuine from those which might be put on, in order to obtain a better compensation; and in forming a judgment, as before remarked, previous conduct and character must be taken into consideration. A malingerer will probably overdo the symptoms; although he will say that he was stunned, he will describe the accident and the events preceding it, which we know is unusual when the accident or blow is severe enough to produce unconsciousness; instead of a mental dulness and apathy, with loss of memory, he will often show mental alertness in describing his symptoms. He may assert that he is unable to walk, or he may simulate a hemiplegia, and yet give none of the characteristic signs of functional or organic paralysis. Not infrequently, however, he has heard of increased knee-jerks, and then the jerk sometimes can be elicited by striking *at* but not *on* the tendon. This anticipation is very suggestive of his mental attitude. Again, spurious clonus can be often detected by making the patient count slowly, then at different rates, while you are obtaining the clonus; it will then be noticed that he is unable to properly attend to two actions at the same time, and the rhythm of the clonus will vary, or the contractions become irregular and halting. A plantar extensor response may be simulated, but by suggestion it can be changed from one side to the other or converted into a flexor response. Asked to touch the tip of his nose with his finger, his eyes being shut, he may fumble about like an ataxic would, but none of the other signs of ataxy would be present.

The less severe forms of traumatic neurasthenia are more difficult to diagnose than those with marked mental symptoms amounting to a Korsakoff psychosis. The following is a fairly typical case of true traumatic neurasthenia.

CASE 4.—Male, occupation, carver, aged 53 years, was knocked down by a taxicab, and admitted to Charing Cross Hospital on April 4th, 1908. On admission he was somewhat dazed and complained of pain over the right eye and behind the left ear. There was no bleeding from nose, ears or mouth. Shortly after admission subconjunctival hæmorrhage developed on the right side. There was pain over the right eye and behind the left ear very severe. Pupils were equal, reacted sluggishly to light. Pulse 92, fairly good character. Temperature 97·6° F. No abnormal nervous signs noted. The patient was quite sensible the next day, and subsequently made an uninterrupted recovery.

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He was examined three years after the accident. He even now gets headaches after rush of business, but otherwise is as well as before the accident. For six months after leaving the hospital he felt very weak and absent-minded. Before the accident he never had any complaints brought against him for slowness in executing orders, but, returning to his place of employment as carver at a restaurant, he was dismissed after a few weeks because he forgot the orders and was slow in executing those he remembered. He was out of permanent work for a year, and three good jobs he lost on account of his inability to remember. He avoids alcohol, and now is quite as well as ever. He obtained £10 as compensation, which was manifestly insufficient.

"*Commotio cerebri*," either the result of concussion without a fractured skull or with a fractured skull, may be followed by a psychasthenia due to a functional disturbance of the brain as an organ of mind. A number of cases, summaries of which are herewith reported, show that a certain group of symptoms follow the period of unconsciousness; the patients are described as being dazed and presenting mental dulness and confusion; they are unable to recollect the circumstances of the accident and the experiences preceding it, occasionally even for some hours preceding it; for months, and even longer in severe cases, there is inability to undertake any prolonged mental effort without fatigue and headache. Generally speaking, there is headache without any cause. Any mental effort requiring sustained attention, deliberation and judgment the subjects of traumatic psychasthenia are unable to undertake, and irresolution and indecision is a frequent result, interfering seriously with any occupation involving responsibility. Thus the bank clerk who could add up correctly and rapidly columns of figures without effort is no longer able to do so. He makes mistakes, and he fears that he will do so. The foreman or overseer of a workshop or a factory now will overlook more than he will oversee. The carver of a large restaurant—Case 4—was unable to attend to the orders of the customers, and for a whole year was out of a situation. The condition is aggravated by insomnia and worry, for these sufferers of traumatic neurasthenia are conscious of their mental deficiency and are filled with apprehension of making mistakes and losing their employment, consequently they are fearful for the future, especially if they have a wife and family to provide for. If there is an inborn insane tendency, delusions of persecution and obsessions may occur.

In severer cases of "*commotio cerebri*" resulting from head injury the symptoms of Korsakoff's psychosis may occur. Thus there may be

marked mental confusion, disorientation of time and space, mistakes in identification of persons, and especially loss of memory of recent events, without delusions or hallucinations. The common cause of Korsakoff's psychosis is chronic alcoholism; it especially affects women, and chronic inebriate women as well as chronic inebriate men are not very infrequently admitted to hospitals and infirmaries having fallen down a flight of stairs or steps, or been knocked down by a vehicle in the street, or received a head injury in a brawl. Delirium tremens or Korsakoff's psychosis may be the result, the former more likely in men and the latter in women. The patient may smell strongly of liquor, or be known to the police as a chronic inebriate—such information helps in a diagnosis. The cases of Korsakoff's psychosis may come on to the asylum, and in some instances the friends attribute the mental condition to a head injury (see Case 8, p. 22), but I have never been satisfied that any of the cases I have seen were really primary traumatic cases. Nevertheless, such cases have been recorded, and do occur. I am indebted to Dr. Elgie for the notes of a case of Korsakoff's psychosis, the result of head injury, which was presumably complicated by localised contusion of the left hemisphere and a patch of meningo-encephalitis beneath the seat of the external injury.

CASE 5.—“*Commotio cerebri*” and contusion of left hemisphere, followed by right-sided epileptiform convulsions, mania, and symptoms of Korsakoff's psychosis. Recovery.

Male, aged 38 years, married, painter. Admitted to Horton Asylum on April 14th, 1909. On March 16th he fell from a ladder to the ground, the distance being about six feet. He was admitted to the West London Hospital the same day in an unconscious condition, with an hæmatoma and ecchymosis over the left parietal and mastoid regions, extending also to the occipital. There were no signs of fracture; no paralysis; pupils equal. Knee-jerks both difficult to obtain and sluggish. He became semi-conscious, and on the 20th had a convulsion of the right side of the body lasting forty seconds. The face was first involved, and there was slight paresis of the orbicularis and tongue muscles of the left side. On the 21st he had a similar attack. He improved slightly afterwards, but on the 26th he became pugnacious and irritable, and on the 27th had to be removed to Fulham Infirmary, whence he was certified and removed to the asylum. (These attacks indicate damage to the left motor area—probably meningo-encephalitis.—F. W. M.)

Condition on admission to asylum.—Fairly well nourished, but pale and

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anæmic: a rough protuberance was noted in the right upper occipital region. Thoracic and abdominal viscera apparently normal.

Nervous system.—No motor impairment noted at first, but afterwards it was observed that he had some obliteration of the right naso-labial fold, and the tongue was slightly protruded to the right. The right eye was not closed as well as the left. Knee-jerks present, left slightly increased; ankle clonus, marked left; plantar reflex, both flexor; light touch normal, heat and cold normal; complete analgesia all over the body, except face; taste and smell both absent; pupils equal, regular, right sluggish; vision normal, fundi normal; hearing, some slight deafness left ear. The patient at first admitted having contracted syphilis, but afterwards denied it.

Mental condition.—He was certified as suffering from confusional insanity, and was dull, very confused, disorientated, and mistook identities. He was very slow of comprehension, rambling and irrelevant in his conversation, talking utter nonsense, and was very amnesic. No hallucinations or delusions were detected. He could not understand written questions and was unable to read, forming words of his own; he was a good example of paralexia. Figures presented no difficulty to him. He could not write correctly from dictation, making mistakes in spelling. He had difficulty in recognising everyday objects—for example, called a match a light-pipe, and explained other objects by dumb show. Progress: He gradually became less confused, and could understand written questions, but still had difficulty in reading, using the wrong word at times, and words of three syllables he had to spell out. His ankle clonus disappeared, but he still had the slight paresis mentioned on admission, and the analgesia persisted. He was eventually discharged as recovered on August 27th, 1909. Treatment: Tonics and potassium iodide were administered, and he appeared to improve rapidly when taking the latter.

This case is interesting from several points of view. A man who probably had had syphilis, who was a painter, and therefore may have had lead in his system, falls from a ladder to the ground. The injury is severe although there are no signs of fracture, for there is a hæmatoma and the man is rendered unconscious; even at the end of four days he is semi-conscious, and then a new symptom indicative of cortical irritation occurs—namely, the convulsive seizure affecting the right side of the body associated with facio-lingual paralysis. I should judge this as being the result of a localised meningo-encephalitis due to contusion of the brain, the result of the injury. Five days later symptoms of mania developed,

for he became pugnacious and irritable; in the interval there had been several convulsive seizures. Later the symptoms of Korsakoff's psychosis developed. Although he was able to recognise numbers and to know their meaning, the subjoined letter shows that he was unable to remember the number of the house he lived in (Fig. 4). There is an apology for his writing, but it was better than his verbal speech. It is quite probable that the defects of verbal and written speech which the notes indicate may be correlated with a profound functional disturbance of the left hemisphere caused by the contusion, which was severe enough to produce irritation and paralytic phenomena in the facio-lingual area of the motor cortex, and which may have affected simultaneously or spread to the whole speech-zone. It is apparent that the anterior and lower part of the speech-zone was more severely affected than the upper and posterior part, for verbal speech did not recover as soon as visual typographical speech. The mental confusion and loss of orientation in time and space, together with the amnesia and the affixing of the wrong names to persons, may be the result of the profound disturbance of the whole speech-zone of the

Dear Jack, I will ~~you~~ send this letter
round to Daisy as I have forgotten our proper
number, hope you are all well. This bad
writing is the fault of my being up in the
hospital the last 7 days
Best wish from
Your brother Harry

FIG. 4.

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left hemisphere. The brain, however, acts as a whole, and a small localised lesion might give rise by diaschisis to a profound disturbance in the whole speech-zone, and this is probably what happened, for had there been an extensive contusion involving the whole speech-zone there would have been paresis of the arm, and recovery would not have occurred as it did. The case shows that an injury producing only visible signs of a localised external contusion may produce a profound mental disturbance. The fact that there was a possibility of a predisposing toxic cause (syphilis or lead) may have had something to do with the establishment of the lesion; moreover, the notes state that potassium iodide led to a rapid improvement, which supports this supposition. Still, the complete recovery and the absence of any definite history of either lead or syphilis leads me to the opinion that the symptoms were all due to contusion of the left hemisphere, combined with commotion of the whole brain. The fact that the localised cerebral symptoms did not come on till four days after the accident is in favour of a localised meningo-encephalitis, and not a subdural or intra-cranial hæmorrhage, as in Case 7, especially as the new symptoms were accompanied by a return of consciousness.

Again, as is well known by the frequency of its happening, a person suffering from severe head injury smelling of alcohol may be taken to the police-station and placed in a cell, and it may or may not be discovered soon enough that drowsiness is not necessarily drunkenness, as the following very interesting case shows:

NOTES BY MR. FENWICK, SURGICAL REGISTRAR.

CASE 6.—Male, aged 39 years, carman. Admitted to Charing Cross Hospital on October 17th, 1910, under the care of Mr. Waterhouse; discharged November 23rd, 1910. Rupture of posterior branch of left meningeal artery.

History.—About 3 p.m. on October 15th, 1910, the patient fell from his van owing to the breaking of a rope by which he was endeavouring to hoist himself up. His head struck the road with force. He lay for a few minutes unconscious and then staggered up. A constable arrived and accused him of being drunk, and, in spite of the expostulations of a gentleman onlooker, marched him off to the police-station, a distance of 400 yards. He was certified as drunk by the divisional surgeon and placed in a cell, but later on, owing to total unconsciousness supervening, he was brought to Charing Cross Hospital on an ambulance. There was ample evidence from people to whom he had just delivered parcels that he

was perfectly sober at the time of the accident. Family history and patient's history revealed nothing of note.

On admission to the hospital, about 7 p.m., the patient was unconscious; his breathing was not stertorous; there was a slight odour of spirits. The eyes rolled from side to side. Both pupils reacted to light, and the left was slightly contracted. The face was pale and the skin clammy. The right side of the face showed obliteration of lines, whereas the left appeared normal, and occasionally the left angle of the mouth was drawn up. The right eye was closed (partial paralysis of the seventh only) and could easily be opened, but the left eye was tightly shut and could only be opened with difficulty. The right arm and leg lay limp, while the left arm and leg were moved occasionally, the left hand being carried to the left side of the head as if there was pain there. (He was said to have had twitchings of the right arm and leg just as he was brought to hospital, but no medical man saw them.) Knee-jerks slightly exaggerated on both sides. Flexor response on right, none on left. No tendon reflexes obtained in upper limbs. Temperature 98° F., pulse 72, not very forcible. The head showed no external evidence of trauma. A few hours later the patient's mental condition improved somewhat; he appeared to recognise his wife, and to attempt to speak, but did not utter any sound.

The next day he was very restless, attempting to get out of bed, and turning from side to side. He appeared to understand simple commands, and would put out his tongue, which deviated to the right. He had incontinence of urine and fæces (large doses of calomel had been given).

Through the following week patient's condition improved slightly; he spoke, but unintelligibly. He was less restless; temperature and pulse were fairly normal; incontinence of urine and fæces remained, so also paralysis down the right side.

Mr. Waterhouse decided to trephine on the 24th. A flap was turned down, and a disc of bone removed over the anterior branch of the middle meningeal, and the anterior margin of a large extra-dural clot was disclosed. This was removed with a scoop through the trephine opening first made, and also through a smaller hole made to facilitate the removal about 2½ in. behind the external auditory meatus. The clot was carefully collected and found to amount to 2 oz.

The patient on recovering from the anæsthetic was found to be sensible, was able to answer questions and to recognise people. Incontinence of fæces and urine ceased; he was able to move the right arm and leg, but these limbs were very weak; paralysis of the face also remained. He

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rapidly made progress, and six days after the operation the arm and leg, although weak, were much stronger than formerly. The facial paralysis was disappearing, and he spoke well. On November 8th, just over a fortnight after the operation, the right hand grip was as good as the left, and the right leg as strong as the other; there was still some paresis of the right side of the face. Tendon reflexes were normal.

He was discharged on November 23rd, and was able to walk well, but it was noted that there was still slight facial paresis, that he suffered from headache on attempting to read, and that a letter written to his wife was almost illegible.

He was again examined July 10th, 1911, nearly eight months after the accident. He had had no fits. For several months after the accident he felt very weak, was absent-minded, and had slight pain or twitching sensations on the left side of the head. He returned to work in February, and at first had difficulty in remembering where to deposit parcels; he would find at the end of the day that he had omitted to deliver several. He gradually improved, and now he considers that he is as good a man as he was before the accident, except that he can now only lift 1 cwt. instead of 1½ cwt. as formerly. He says that for a month after leaving hospital his writing was very bad, and that he had difficulty in spelling—"he couldn't think how to write."

When the patient left hospital he could only recollect events on the day of the accident up to lunch time, but recollection gradually returned, and about a month later he recollected the rope breaking, but not rising from the ground. He recollected being walked by the constable to the police-station, and asking the inspector what he was charged with, and being told that "he would be alright in a hour or so." His mind was a blank from that time up to when he found himself in Charing Cross Hospital after the operation. He has avoided alcohol, because of the warnings given him on leaving hospital.

Nervous system.—Pupils equal and react normally. No sign of paralysis anywhere. Face muscles act perfectly on both sides. Grip of the right hand as good as the left, and he walked well. Reflexes normal throughout. He received no compensation whatever, but was allowed half pay, and his job was kept open for him.

In this case there was only a slight "commotio cerebri"; the developing symptoms were mainly due to the compression caused by the extravasated blood. There was an anaemia of the brain cortex due to the escaped blood, causing loss of consciousness, together with the local effects

of direct pressure. During this period of cerebral anæmia the neurons were not acting because there was oxygen insufficiency, and the mind for that period remained a blank. The brain failed as a perceptor as well as a recollector during the period of compression. But it will be noted that he now remembers nearly all the circumstances of the accident and what followed, so that the "*commotio cerebri*" was slight.

Concussion interferes, therefore, with the neurons directly in their vital reactions to the circumambient medium, whereas compression interferes with the oxygen supply to the circumambient medium. Remove the cause of the latter and the mind recovers.

Another question of great importance besides the immediate diagnosis is the prognosis, for a head injury which has produced "*commotio cerebri*," or concussion with fracture resulting in traumatic neurasthenia, may eventually terminate in an incurable and fatal brain disease. Several months may elapse before symptoms of traumatic epilepsy or general paralysis come on; and if such occurred within a few months rather than immediately after, or a long time after, it might be presumed that the head injury was a determining factor in the onset of the disease (*vide* Cases 16 and 17). Indeed, it might be affirmed, and with good reason, that had not the injury occurred, the epilepsy or the paralytic dementia would not have affected the patient (Case 14). Yet, as we shall see from hospital cases and asylum statistics, head injury *per se* is not a frequent cause of epilepsy, and modern investigation shows that syphilis is an essential factor in the production of general paralysis, consequently contributory determining causes must co-operate, and among these are occasionally head injuries. Still, as with epilepsy, there is in general paralysis always the difficulty of discriminating between cause and effect.

The first manifestation of both these diseases may be a sudden lapse of consciousness—a fit or seizure—whereby the individual may sustain a head injury. The loss of consciousness following the head injury may be due to the disease and not to the trauma. Thus, a bricklayer may fall from a ladder, or an engineer's mechanic may be injured by machinery, owing to a pre-existing disease causing a lapse of consciousness; later, if he developed epilepsy or general paralysis and claimed compensation, it might be asserted with justice that the accident was in consequence of a pre-existing disease, although there was no very definite evidence to prove that he had suffered from it. Such rebutting evidence in a claim for compensation, however, could not be made if a brick had fallen on the man's head, or if a head injury resulted from the breaking of a machine,

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as in Case 3. Again, both epileptics and general paralytics in the early maniacal stage are impulsive and quarrelsome; they are therefore liable to receive head injuries from blows or from being knocked down, and the wife or friends may attribute the disease to the blow.

Before dealing more especially with traumatic epilepsy, general paralysis, meningitis, tumours, and other organic diseases which may follow and be caused by head injury, I will refer to statistics of head injury in asylum practice.

STATISTICS OF HEAD INJURY IN RELATION TO MENTAL DISEASES.

Dr. Stansfield, the Superintendent of Bexley Asylum, kindly gave me the following information :

In 7400 admissions since the opening of the asylum there were 16 male cases and 20 female cases where head injury might be considered as a contributory or determining cause. He also informed me that it was his opinion that head injury as a prime cause of mental disease was extremely rare; he could only recall one of the cases where it thus acted (Case 3). Seeing that the notes taken at this asylum have been very carefully collated, this information is very valuable. But similar results were obtained at other asylums. Thus, Dr. Daniel could only obtain a history of head injury in 7 out of 919 female cases admitted to Hanwell Asylum in four years—1907–1911 inclusive. The cases were as follows :

CASE 7.—Congenital syphilitic imbecile, with interstitial keratitis and squint, daughter of a drunken imbecile mother. The child was always backward, and suffered from convulsions in infancy; the mother attributed her mental state to a blow on the head. It is probable that this was a mere coincidence, and had no causal relationship.

CASE 8.—A married woman, a cook by occupation, with a history of alcoholic neuritis and Korsakoff's psychosis, received a blow on the head. There was no sign of head injury on admission; later on she died of chronic interstitial nephritis and valvular disease of the heart. Probably the head injury was a coincidence, but there may have been some causal connection between the head injury and the onset of the psychosis.

CASE 9.—A girl, aged 17 years. Admitted to asylum suffering from insanity of adolescence (*dementia præcox*); she received a blow on the head at the age of eight. Probably no correlation.

CASE 10.—A girl, aged 8 years on admission, fell off a swing at the age of five. A year later had an attack of biting and screaming; previously she had been normally developed physically and mentally. There is a

step-sister, an epileptic imbecile, in Horton Asylum. The father is intemperate. It is very doubtful whether there is any correlation between the head injury, of which there are no signs, and the mental affection.

CASE 11.—A woman, aged 69 years. Admitted February 24th, 1910. There is a history of her having been struck on the head with a flat-iron, to which her dementia was attributed by the friends; but there was a history of her having had a fit two or three months before the head injury, and she lost her memory in consequence. Besides, there had been several previous attacks indicative of arterio-sclerosis and thrombosis with softening. So that the head injury can only be accounted as a contributory factor in the production of the dementia.

CASE 12.—A single woman, aged 48 years, had a bicycle accident twelve months prior to admission to the asylum; the accident was followed by insomnia, giddiness at times, defective memory, and headache with melancholic depression. In this case her insanity may be attributed to the climacteric period, and the head injury was an important determining cause.

CASE 13.—A girl, aged 15 years, admitted November 3rd, 1910, with a history of injury to the back of the head five weeks before admission. The certificate stated that she was a congenital imbecile from birth. The paternal uncle died at Cane Hill Asylum. No doubt the injury produced acute symptoms, for she was taken to the infirmary, where meningitis was diagnosed, but these have passed off while in the asylum.

I have given a brief summary of these seven Hanwell cases, in order to show how very difficult it is to assert that injury ever acts as more than a contributory cause in the production of insanity, and is rare even as a co-efficient.

Inquiries at other asylums help to substantiate this statement. Thus, Sir James Moody has kindly made an inquiry, and informed me that of 984 male patients at Cane Hill there was only a history of head injury in 17, and when I analysed these cases I came to the conclusion that very few of the 17 had a causal relationship. At the Manor Asylum, Horton, Dr. White has been good enough to carefully examine all the case-books since the asylum has been opened. All cases in which there is any mention of injury of any kind (not necessarily head injury) at any time previous to the onset of the mental disease have been listed, and yet we only find 71 out of 2561 cases = 2·7 per cent.

I have been carefully through the records of these cases, which are nearly all females, and I find that in the majority of the cases the notes

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prove no relationship between the injury and the attack of insanity. Occasionally one finds an old woman is knocked or falls down in consequence of senility or senility and drink; following this there is apparently a development of mania or melancholia or senile dementia, but how far the injury had been the cause or the consequence of the mental condition it is almost impossible to say, for the notes do not tell as a rule whether the patient was rendered unconscious, or whether she required hospital treatment or not. There are one or two cases of interest, however.

CASE 14.—Woman, aged 48 years, was admitted suffering from general paralysis of the insane. Seven months before admission to the asylum in June, 1908, and five months before the symptoms of insanity became manifest, an iron saucepan fell on her head. There is no history of insanity, intemperance, or tuberculosis in the woman herself or her family. Was this blow, then, the cause of the disease? It was only the determining cause at the most, for there was a definite history of her having contracted syphilis after marriage.

CASE 15.—A. L. P—, aged 22 years, a congenital imbecile, fell from a swing when five years old, suffered from concussion, and was an in-patient at Guy's Hospital for about six weeks. Quite a few cases of epileptic or imbecile children are recorded as having fallen from a swing, and to this the mental disorder was attributed by the parents, but the medical officers who recorded these notes either were unable to pursue the inquiry further, or did not take the trouble to interview the friends and ascertain more precise particulars as to whether the scalp was cut and required stitches, whether the child was unconscious, or whether there was any evidence of fits before the injury.

I will now pass on to consider the analysis of the case-book and *post-mortem* notes of 2090 autopsies made by myself or my assistants at Claybury Asylum:

In only one of the cases could the insanity have resulted from the head injury as the prime cause; in some it was possibly an exciting or accelerating factor. More than half the cases occurred in old people, suffering in many instances from brain conditions due to cerebral softening or vascular disease. The notes as a rule do not state whether the injury was severe, or whether there was a loss of consciousness, or, in fact, any information which would allow one to decide a causal relationship between the insanity and the head injury. At the autopsy in only one (Case 2) was there any evidence of fracture or severe injury of the skull.

STATISTICS OF 2090 AUTOPSIES IN RELATION TO HEAD INJURY.

In 33 cases out of 1057 female necropsies at Claybury there was a history of head injury of some kind at some period of life in 3·1 per cent.

Melancholia	9 cases
Senile dementia	7 „
General paralysis	4 „
Mania	4 „
Alcoholic insanity	3 „
Recurrent insanity	3 „
Epilepsy with insanity or imbecility	3 „

In 1033 male necropsies there were 56 cases (5·4 per cent.) in which the notes stated that the patients at some period of their lives had received head injuries. Nearly one half of these cases were general paralytics; in fact, it is the excess of paralytics which has raised the percentage of head injuries in males so much above that in females.

General paralysis	26 cases
Senile dementia	11 „
Melancholia	7 „
Mania	4 „
Epilepsy with insanity	3 „
Recurrent insanity	2 „
Congenital imbecility	1 case
Tumour cerebri	1 „
Internal hydrocephalus, fracture of base	1 „
Alcoholic insanity	0 „

In only one case was a condition of injury found *post mortem* which could have been the essential cause of the insanity; this was so in the case of internal hydrocephalus secondary to basic meningitis, the result of fracture of the base (see Case 2). In not a few of the cases of general paralysis head injury may have accelerated the course of the disease, but there is no evidence in any of the cases of a certain causal connection between the head injury and the onset of the symptoms; and there was no case which showed that the patient was mentally perfect before the accident or injury. In many of the cases the time prior to the accident or the nature of the accident was so indefinite as to afford no support to the opinion that the head injury was related to the disease in a causal way. There was often evidence that the disease had directly or indirectly caused the injury. Thus a lapse of consciousness led to a

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fall, or a blow was received in a quarrel in the maniacal stage. Such injuries may undoubtedly have accelerated the progress of the disease.

STATISTICS RELATING TO GENERAL PARALYSIS AND TRAUMA.

It has been stated that statistics show that cases of general paralysis in which there is a history of trauma run a more rapid course; individual cases occasionally occur where it may be safely affirmed that head injury has accelerated the course of the disease. Gudden's statistics pointed to the fact that the average age of onset of general paralysis was less in cases with head injury. With a view of ascertaining if this accorded with our experience at Claybury, I have collected the statistics of general paralysis with and without a history of head injury; and I may here remark that the notes regarding a history of head injury having occurred are more likely to be contained in the case-book than the history of any other ætiological cause, for the friends are able usually to afford information on this point, whereas in such matters as hereditary insanity and history of syphilis no reliable information can be obtained in a large number of cases, unless the friends are personally seen and considerable trouble taken to make inquiries; even then difficulties must arise.

AUTOPSIES ON CASES OF GENERAL PARALYSIS.

There were 21 male private cases, and the average age at death was 46·5; among these there was not one with a history of head injury. There were 235 male pauper paralytics in whom there was no history of head injury in the notes, and the average age at death was 43·5; there were 29 male pauper paralytics with a history of head injury of one kind or another occurring at all periods during the life of the individual; the majority, however, are stated to have occurred within a few months to a few years of the admission of the case to the asylum; the average age at death in these 29 cases was almost the same as in those with no history of head injury—namely 43·3. In only a very few instances does there seem to be any causal relationship between the injury and the precipitation of the onset, or the acceleration of the course of the disease.

In 1033 male necropsies there were 61 with a history of trauma, and of these 29 were cases of general paralysis (the total number of male paralytic cases was 317), making about 9 per cent. general paralytics in which there is some history of a blow or a fall on the head. Of the 111 female general

paralytics, there were only 4 with a history of trauma, therefore less than 4 per cent.

I have carefully considered the following points in those cases where trauma has been the reported cause, or contributory cause, of the paralysis; and the evidence afforded by the notes in the case-books in my judgment does not in a single instance allow one to assume that the head injury was the *principal* cause of the general paralysis from which the patient died. In some instances the destructive changes in the brain at death, together with the history and clinical symptoms, indicated a duration longer than the period of time between the date of injury and the date of death; in others—and they are not a few—the time elapsing between the date of injury and the onset of symptoms was too long to be accounted responsible as an exciting cause of the disease; in a great number of the cases the nature of the injury, whether severe enough to produce a temporary loss of consciousness or to require medical treatment, is not given, nor is the time and date of the injury mentioned, so that the influence of the injury in the production of the mental disease can never be appraised.

As a general result of my investigations I have come to the conclusion that head injury as an exciting cause was not of much importance either in causing the onset of general paralysis or in accelerating the symptoms. At the same time I have met with a few cases (see Cases 3 and 14) where undoubtedly head injury may have been the determining cause of the onset of the symptoms, and it is not unreasonable to suppose that a syphilitic, if he or she had not received some exciting cause, such as a blow on the head, might never have developed general paralysis, but these cases are rare.

General paralysis may not be discovered until an accident or a head injury takes the patient to a hospital or infirmary. Thus I have known the case of a prostitute who received a blow in a drunken brawl. She was already a paralytic at large, but not until she was taken to the hospital or infirmary on account of the injury was the nature of her affection recognised; she was then sent to the asylum.

My figures do not agree with those of Gudden; as you observe, there is practically no difference in the average age of death of those cases with a history of trauma and those without. There is one essential cause of general paralysis, and that is syphilis. All conditions which lead in a non-syphilitic subject to neurasthenia may act as exciting and contributory factors; they are sexual excesses, head injuries, alcoholism, speculating, gambling, business worries, leading to prolonged mental excitement and

insomnia, in fact all forms of nervous excitement, singly or combined, which will lead to an exhausted nervous system, especially when acting upon an inborn neurotic and erotic temperament in the subject of acquired or inherited syphilis.

HEAD INJURY IN RELATION TO TRAUMATIC EPILEPSY.

In considering the statistics of head injury in relation to epilepsy a large proportion of the cases in which there is a history of trauma as a cause must be discounted, for the friends fail to discriminate cause and effect; again, many congenital imbecile epileptics suffer from falls or injury, and that which was due to an inborn taint or defect is attributed to the fall or injury. At the epileptic colony, Ewell, there are 800 cases on the books, and of these I am informed by Dr. Collins, the Superintendent, there are, roughly speaking, 160 cases in which the friends have thought fit to mention injury—a very much higher percentage than that obtained among general paralytics, and still higher than that met with in other forms of insanity. Dr. Collins said there were about 6 cases out of the 160 which might be considered of traumatic origin. There is no doubt that trauma may be a cause of epilepsy, but how far the head injury is the primary and sole determining cause or merely an exciting or contributory factor in a person predisposed by an inborn taint, by alcoholism, or syphilis is difficult to decide. Very often an epileptic for some long time may have been manifesting signs of the disease unbeknown to relatives and friends; he may have had *petit mal* attacks or fits during sleep; then perhaps while at his employment he falls down in a fit and injures his head, perhaps severely, and remains unconscious for some time. His symptoms may now be exaggerated, the fits being more severe; or, owing to the accident, his friends notice his mental and bodily condition more closely, and naturally attribute all the symptoms they now see and the fits which subsequently occur to the head injury. Often the circumstantial evidence appears very convincing that the head injury was the cause, but, did we know all the facts, many cases in which injury was the *apparent* cause would be found to be really not due to the injury. Thus an epileptic imbecile died at Claybury aged 24 years. She was said to have had a blow on the head at the age of nine, and the fits and amentia were attributed to the injury. At the autopsy I found bilateral microgyria and porencephalon—a congenital defect which is a not infrequent cause of epileptic imbecility. The head injury could have had no part in the production of this defect.

Severe head injuries causing fracture of the skull and unconsciousness, some necessitating operative interference, may recover completely if they do not die within a short time of the accident; for a variable time afterwards they may suffer from the symptoms of traumatic psychasthenia, but they do not develop epilepsy unless there is some inborn or acquired condition favouring convulsive attacks. If, however, there is an irritative lesion of the cortex in or near the motor area a Jacksonian epilepsy may be the result, and the epileptiform convulsions of a typical Jacksonian type may by repetition spread so rapidly over the whole excitable cortex of both hemispheres that the fits become indistinguishable from essential epilepsy. If head injury causes a traumatic epilepsy coming on very soon after the injury, a successful operation should cause the fits to stop. One well-observed case (in which all predisposing causes can be eliminated) cured by operation would be more convincing than a large number of doubtful and badly observed cases. Raymond has asserted that traumatism can produce a partial cortical epilepsy without any appreciable lesions of the motor cortex. Pitres and Kocher adopt a mixed theory that compression plays a predisposing rôle, the cerebro-spinal fluid being under pressure.

Alexander has recently performed the operation of fenestrating the dura in epilepsy. Some of his cases were of traumatic origin, and he has found the membranes thickened over the motor area and an accumulation of fluid. Epilepsy may be the result of injury to the cranial vault; splinters of the inner table are driven into the brain or a cicatricial thickening of the membranes act as a focus of irritative discharge. It is probable that one of these conditions exists in the following case.

CASE 16.—An Italian, aged 41 years, was admitted to Colney Hatch Asylum two years ago. He has a fit every two or three months; he knows when they are coming on, for he has a spasm in the left foot, but faints and falls down unconscious. The fits generally occur at night; he does not know how long he remains unconscious. The fits always begin in the left leg. Five years ago he fell down a lift while acting as cook in a private family. He was taken unconscious to the hospital (Charing Cross?) and was trephined. There is a trephine hole, 2 in. by 2½ in., just above the *left* ear and 2 in. from the vertex. After two months he was transferred to the Chelsea Infirmary, where he remained two years. Three or four months after the accident the fits commenced. There is no paralysis of the right arm, leg, or face; the only evidence of motor affection is inability to close the right eye independently of the left. Knee-jerks present both sides, not exaggerated. He is a born left-handed man, and he says that he is

unable to use his left hand as well as before the injury. These fits, always beginning with spasm in the left leg, suggest either a splintering of the inner table by *contrecoup* or some thickening and cicatrisation of the meninges and cortex, the result of contusion by *contrecoup*. There was no history of epilepsy or insanity or any acquired cause or factors obtainable in this case.

CASE 17.—A male, aged 20 years, admitted to Colony Hatch Asylum at the age of nineteen. Since eleven years of age he has suffered from epileptic fits. A gang of boys struck him over the left frontal eminence with a piece of iron. He walked home, and attended the Middlesex Hospital as an out-patient for six weeks; then he was admitted and trephined over the seat of the injury; only a small circular opening was made, not more than an inch in diameter. Two years after he left the hospital the fits came on. He knows when they are coming on by his head turning to the right; he gives a cry and falls down; tonic spasms are followed by clonic spasms. He does not fall into a sleep, but soon gets up; he is a little irritable, otherwise there are no psychic effects before or after the fits. Neither parents suffered from epilepsy, but the father was at Hanwell Asylum, and died there.

ORGANIC DISEASES DETERMINED BY TRAUMA.

I have seen several cases of head injury in syphilitic subjects lead to a *gummatous pachymeningitis*. I have published two cases in which, following a blow on the head in the region of the parietal eminence, severe headache, sickness, and flashes of bright light on the same side as the localised tenderness, together with pain on pressure at the seat of the injury, occurred. In both cases mercurial inunction, local and general, combined with large doses of potassium iodide, soon relieved the symptoms and eventually cured the patients. I have also published the notes of a case of meningo-myelitis syphilitica determined by trauma.

Tuberculous meningitis.—Most physicians to children's hospitals consider head injuries, particularly falls, as an important determining cause of tuberculous meningitis in young children and infants.

Tumours.—Cerebral tumours—tuberculous, simple, and malignant—are said to be determined by falls or blows on the head; the only tumour which I should definitely associate with injury would be a gumma, which, as we know, starts from the meninges. Still, if there is produced by the injury a *locus minoris resistentiæ* with congestive stasis and extravasation, there

is no reason why, as pointed out by Dr. Colquhoun, of Dunedin, a suitable nidus for the development of parasitic organisms or cancer-germs is not provided, and on that account head injuries may be the determining cause of growths of all kinds. I may say, however, that there was only one case of growth in the 89 cases of head injury among the 2090 autopsies, which is about the same proportion as among the non-traumatic cases.

Meningitis, non-tuberculous.—Fractures of the base of the skull may occasionally give rise to an acute or chronic meningitis (see Case 2).

TRAUMA AND GENERAL PARALYSIS.

I will now pass on to a consideration of general paralysis of the insane—the most important organic disease from a medico-legal point of view. In fact, a number of cases of claim under the Workmen's Compensation Act have occurred recently in the London County Asylums, brief abstracts of which I will give, as each one illustrates some one or more points of medico-legal interest.

SUMMARIES OF SOME RECENT GENERAL PARALYTIC CASES IN WHICH CLAIMS FOR COMPENSATION WERE MADE.

(1) *Compromised claim for compensation.*—A man who was employed by a newspaper company delivering papers was knocked off his bicycle by collision with a car; shortly after the accident he was sent to Colney Hatch Asylum, and died two months later. An inquest was held, and the finding of the jury was that the injury had precipitated but had not caused the disease; this conclusion was arrived at from the *post-mortem* examination, as the changes in the brain were much too far advanced to have occurred within the short period of time since the accident.

(2) *Unsuccessful claim for compensation.*—A builder's clerk received a slight head injury; while unloading wooden bricks one bounded up and struck him on the head; he walked to the hospital and had a slight scalp wound dressed. Shortly after he was admitted to Claybury Asylum, where he died two months after the accident. At the autopsy, a recent *pachymeningitis hæmorrhagica* was found. The question arose, was the pachymeningitis the result of the blow on the head with the wooden brick? The wife admitted mental derangement had existed for some time prior to the accident. The hæmorrhage appeared more recent than two months. Many cases of general paralysis show *pachymeningitis hæmorrhagica* in which

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there is no history of trauma. Consequently the wife was unsuccessful in the claim for compensation.

(3) *Compromise by the railway company in an action by the wife of a railway guard.*—The man was admitted to Cane Hill Asylum suffering from general paralysis. The wife attributed the disease to an injury sustained in a shunting accident. Evidence was obtained by the company to the effect that prior to the accident the man had been strange in his conduct, and therefore the injury had not produced the disease. As rebutting evidence it was shown that the medical adviser to the company had seen the man and examined him, and had ordered him back to his work. The case, therefore, did not come into court, the company compromising the claim.

(4) *Successful action for damages against a railway company by the wife.*—The employee of the company was engaged in unloading a truck; he slipped, it is said, and struck his head against an iron bar. According to the evidence of the doctor who attended him, the blow was a slight one and not sufficient to set up organic brain disease. Several doctors were called to give evidence, including a specialist who saw the man at the hospital but did not remember the case. He expressed the opinion that syphilis was an essential factor, but that a blow might act as the exciting cause. The county court judge gave as his judgment: "It is clear to my mind that the blow did have an effect upon him, and I do not see my way in the evidence before me to say that the effect of the blow has been sufficiently compensated for, and that had there been no blow the man would have been in the condition he is. In these circumstances I put no period to the effect on the incapacity as the result of the accident, and I think the company should pay 13s. 8d. per week from the date on which the last payment was made and continue to pay."

(5) *Unsuccessful action by wife for compensation.*—This case was of interest for several reasons. It was proved that the man met with the head injury owing to his interfering with another man's work. There was a definite history of syphilis, and both the cerebro-spinal fluid and the blood were examined by an expert, and he gave evidence in court to the effect that both gave a positive Wassermann reaction. Judgment was given against the wife, the reason being that the man had not met with the accident while attending to *his* occupation; moreover, the judge remarked that he was not satisfied that the injury was the immediate cause of the insanity.

No doubt the Wassermann reaction will in future play an important

part in medico-legal actions arising from claims for compensation in organic disease of the nervous system. It is therefore important that some definite understanding should be arrived at as to the methods to be employed and the value of the test. From a considerable experience at the Claybury Laboratory, based upon observations made by my assistant,* Dr. Candler, and Dr. Henderson Smith, of the Lister Institute, upon cases under my care at Charing Cross Hospital and in the London County Asylums, I have come to the following conclusions:

- (1) The original Wassermann method is the most reliable.
- (2) Four dilutions at least should be made.
- (3) In the case of the cerebro-spinal fluid not less than 0.5 c.cm. should be used.
- (4) If the blood-serum does not give a positive result, the cerebro-spinal fluid will be negative. On the other hand, if the cerebro-spinal fluid gives a positive result, the blood-serum will also.
- (5) In general paralysis 97 per cent. of the cases gave a positive result with the cerebro-spinal fluid, accompanied by a lymphocytosis. The correctness of this percentage, which is similar to that of Plaut, has been proved by *post-mortem* macroscopic, and if necessary, microscopic, investigation of a large number of general cases of paralysis.
- (6) If the blood-serum gives a positive Wassermann reaction, and the cerebro-spinal fluid shows a lymphocytosis but gives a negative Wassermann reaction, it is greatly in favour of the disease not being either general paralysis or tabes, but a gummatous meningitis which may clinically be a pseudo-general paralysis or pseudo-tabes case. I have published several cases in my 'Morison Lectures' proving the truth of this statement.
- (7) It is not safe always to assume that a case is not syphilitic, or at any rate will not yield to anti-syphilitic remedies, because the blood-serum yields on several occasions a negative reaction. I have occasionally seen instances in support of this statement. A case of ophthalmoplegia interna and externa gave a negative serum reaction on several occasions, yet in three weeks was completely cured by mercurial inunction and large doses of iodide.
- (8) The Wassermann reaction may disappear under the influence of "606" or mercury and again reappear.
- (9) The serum reaction is not nearly so significant as that of the cerebro-spinal fluid from a diagnostic point of view.

* A full report of this investigation by Dr. Candler will appear shortly.

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(10) The examination of the cerebro-spinal fluid in general paralysis is most valuable; it may be necessary to make lumbar puncture more than once to obtain the reaction. Occasionally, but very rarely, even then a negative reaction may occur; this may be due to excess of cholesterol, at least that is the explanation I should offer tentatively. Cholesterol is always present when nervous tissue is breaking down; this possesses anti-hæmolytic properties, consequently excess might interfere with the action of the globulin substance that causes the deviation of the complement. This globulin may be removed by dialysis, by heating, or by precipitation with alcohol, and the fluid then no longer gives a positive reaction. There are many other points to which I might have called attention, but I will content myself by thanking the superintendents of the London County Asylums and my surgical colleagues at Charing Cross Hospital for the kind assistance they have given me. Also particularly I desire to thank Mr. Fenwick, surgical registrar, for kindly interviewing a number of patients who had been admitted at some previous time for head injury and who had been discharged. A summary of these cases is appended.

THE AFTER-RESULTS OF 13 CASES OF SEVERE HEAD INJURY ADMITTED TO CHARING CROSS HOSPITAL.

None of these Cases of Fracture suffered later from Fits.

(1) Rupture of middle meningeal posterior branch. Operation; recovery. Seen eight months later; memory had returned for all events which happened up to the time when signs of compression occurred, but during this time till operation "all is a blank."

(2) Fractured base. Extra-dural and subdural hæmorrhage (?) Rupture of cavernous sinus. Two operations. Dementia, persistent; man in Horton Asylum.

(3) Compound depressed fracture of vault. Operation. Nine months after accident, memory enfeebled, liable to severe headaches; depressed and nervous.

*(4) Fractured base. One year after operation, recovered in every way, except unable to remember well.

†(5) Fracture of base and vault. No operation. Eight months after

* Loss of consciousness at the time of accident.

† Continuance of unconsciousness for some hours after admission.

accident, headache, weakness, dizziness, nervous and depressed, memory very bad. Four months later improved and returned to work.

†(6) Fractured base. Two years after, severe headache, worse if worried or subjected to noise; lack of power of attention, and memory much impaired.

†(7) Concussion. One year ten months after accident, lack of concentration of attention, subject to headaches, unable to take interest in matters.

*(8) Fractured base. Three years after accident, severe headache after rush of business, unable to give sustained attention for six months, out of work for one year. Gradual improvement; now quite well.

†(9) Fractured base. Two and a half years after, memory still very bad; cannot recollect names of friends or places; insomnia, but no headache.

†(10) Fractured base and concussion; returned to work three weeks after accident. Nine months after, no effects now.

*(11) Fractured base. Three years and four months after, "as good a man as ever"; out of work four months.

*(12) Depressed compound fracture of frontal bone. Operation, elevation. Discharged nine days after admission, recovered; five years after accident still quite normal.

*(13) Compound depressed fracture of vault. Extra-dural hæmorrhage. Operation; complete recovery.

* Loss of consciousness at the time of accident.

† Continuance of unconsciousness for some hours after admission.

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IS INSANITY ON THE INCREASE?*

BY

F. W. MOTT, M.D., F.R.C.P., F.R.S.,

Pathologist to the London County Asylums, and Senior Physician
to Charing Cross Hospital.

THE subject of this paper is an important question to the ratepayer and the race; it can only be answered by a careful consideration and comparison of published statistics and facts regarding insanity, registered and unregistered, in the past and present. Moreover, if insanity be greatly on the increase, as a superficial glance at the rapid rate of increase of registered cases during the past twenty or thirty years would indicate, the causes for the increase should be apparent in the answers to two questions. (1) Have the conditions required for certification undergone any change and is the standard of sanity continually being raised, so that a larger number of individuals are admitted and detained in asylums? The corollary to this is the question of the rapid increase of provision for housing and maintaining persons of unsound mind. (2) If there be the rapid increase of insanity among the population that the growth of the certified insane with increased provision appears to show, what are the causes of this increase? On the one hand the eugenists would associate it with the tendency of modern civilisation to interfere with natural selection and survival of the fittest whereby poor types are weeded out; and to them the inborn factor is paramount; on the other hand the social reformer would associate the increase with drink, poverty, overcrowding and disease. It is the old question of the relative importance of Nature and Nurture in which is involved the great problem of heredity and the transmission of acquired characters. Are acquired characters transmissible? The eugenist should allow that good raw material may be found in all classes and there is abundance of it spoiled by a bad environment. The social reformer should exercise discrimination between good and bad raw material, and recognise the fundamental teaching of heredity that "like tends to beget like" and that the most he can do by his efforts is to prevent good material being spoilt and bad material being made worse. Education, sanitation, feeding, and the like, can through providing a healthy

* A paper read before the Sociological Society, October 29, 1912.

body develop and improve such potential mental energy as the individual possesses; but if there is an inborn failure of sagacity the improved environment cannot bring it out.

THE GREAT INCREASE OF REGISTERED INSANITY.

The charts I shall first show to indicate the increase of registered insanity are taken from the Lunacy Commissioners' Report for this year. The first chart shows the total number of insane persons in England and Wales reported to be under care on the 1st of January in each year specified; and of those in the pauper and private classes respectively. There has been a steady rise of all classes since 1864, viz., from 44,795 to 135,661; the paupers have more than trebled in numbers, the private cases have doubled their numbers. (Fig. 1.)

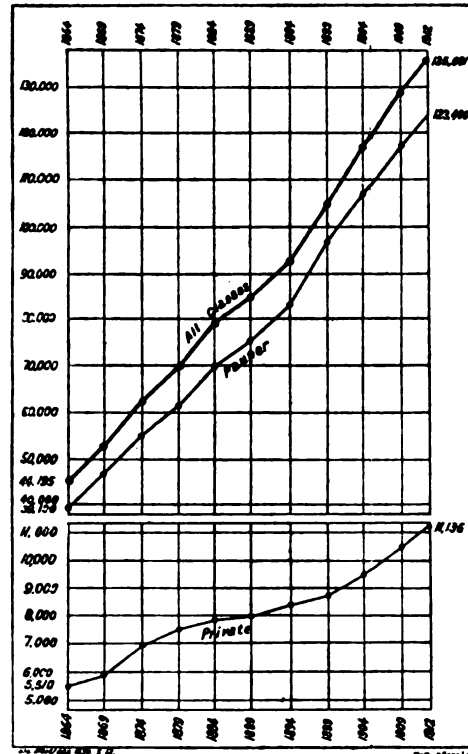


FIGURE 1.

CHART NO. 1. Showing Total number of Insane Persons in England and Wales reported to be under care on the 1st January in each year specified; and of those in the Pauper and Private classes respectively.

The next chart gives the comparative variations in the proportions of the insane in England and Wales (and of the

pauper and private classes respectively) to the total population, 1859 to 1912. It will be observed that the registered insane have increased from 18·7 per 10,000 of all classes in 1859 to 37·1 in 1912. Practically the registered insane per 10,000 of the population have doubled in numbers in fifty years. This does not however necessarily mean that lunacy has doubled in this period in the total population. (Fig. 2.) We notice in this chart that whereas

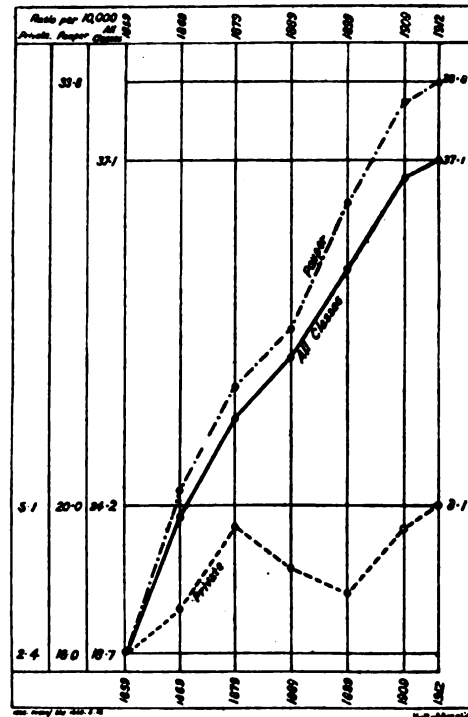


FIGURE 2.

CHART No. 2. Showing comparative variations in the proportion of the insane in England and Wales (and of the Pauper and Private classes respectively), to Total Population, 1859 to 1912.

the pauper class has mounted from 16·0 per 10,000 to 33·8 rather more than double, the private class has only increased from 2·4 per 10,000 to 3·1.

Chart 3 illustrates the rate of insane per cent. of (a) population of England and Wales; (b) of insane community; (c) of the yearly admission to care; (d) of the ratio of insane to the population; and (e) of the ratio of admissions to population 1869—1911-12. Comparing first the annual admissions with the total insane we observe that during the last eight years although the number per 10,000 of the population has risen from 110 to 155·1, the annual admissions have varied between 108 and 110 (the opening of one

or two new large asylums would be sufficient to account for this small variation). When we look at the lower three curves we find that there is a parallelism between the increase of the mean population and the increase of the total insane; but the lowest curve shows that there has been a steady fall in the admissions ratio since 1902 when it attained its maximum. It was at this period that a great increase of housing provision for the insane occurred in London and other parts of the country. (Fig. 3.)

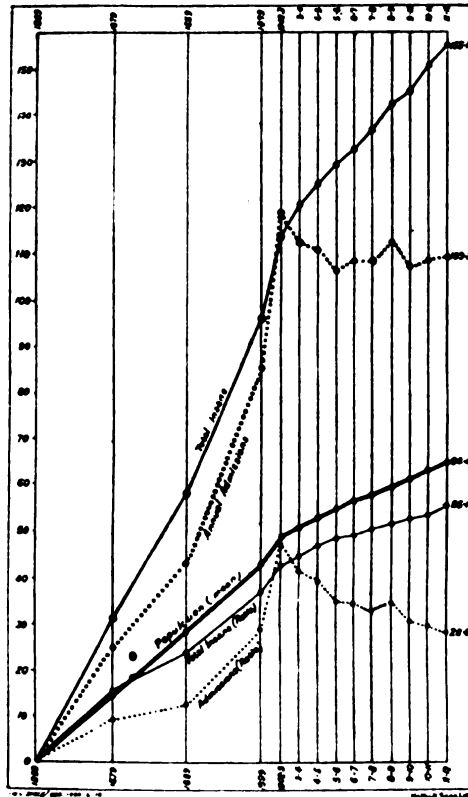


FIGURE 3.

CHART NO. 3. To illustrate Rate of Insane per cent. of (a) Population of England and Wales; (b) of Insane Community; (c) of the yearly Admissions to Care; (d) of the Ratio of Insane to Population; and (e) of the Ratio of Admissions to Population 1869 to 1911-12.

In the report the Commissioners allude to the fall in the admission rate; they say it is somewhat encouraging to find that whereas the advance in population between the estimated average of 1902-06 and that of the next quinquennial period 1907-11 is 5.3 per cent., and on the same basis of comparison, the number of insane under care shows an increase of 0.6 per cent.; *there has as regards the numbers admitted to care been no increase at all, but*

an actual decline. In their last report they dwelt on the factor of "accumulation" as mainly contributing to the increase, believing that the extent to which it operates in the latter is often not fully appreciated, whilst the facts just cited tend to show that of late years at least, there has been no growth of the numbers of insane persons *admitted* to care, the proportion of which to the total under care has fallen from 26·5 to 20·5 per cent. within the past ten years.

REGISTERED INSANITY IN THE COUNTY OF LONDON.

The great increase in the registered insanity in the County of London is the subject which I am especially interested in, as Pathologist to the London County Asylums, for the great increase which is shown in this chart naturally requires explanation from one whose duty it is to investigate the causes of insanity. We observe that in spite of an almost stationary population the increase of registered insanity has gone up by leaps and bounds. In the last twenty years it has risen as this chart shows, from 16,000 to 27,500. (Fig. 4.) In the last twelve years the population of the

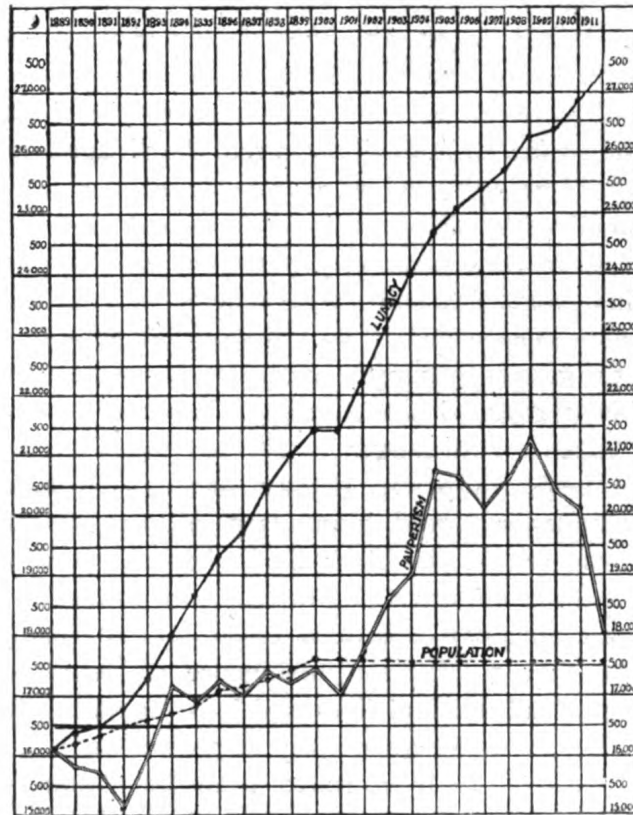


FIGURE 4.

county has been stationary, but the registered insanity has increased from 23,500 to 27,500; that is to say, in a stationary population registered lunacy has increased 15 per cent. in twelve years. Although for some years the pauper curve rose with the lunacy curve, yet during the last three years there has been a steady fall; this is doubtless due to the effect of old-age pensions. Now we have to inquire what are the causes which have led to this increase of registered lunacy throughout the country and in London in particular.

CAUSES OF INCREASED REGISTRATION AND CONSEQUENT ACCUMULATION IN ASYLUMS.

A special investigation made by the Royal Commission on the Feeble-minded in England and Wales disclosed the fact that 0·46 per cent. of the total population were mental defectives and were not at present registered; they are therefore almost as numerous as the registered insane. It has been calculated that if the same percentage holds good for the population of London with its 4,522,961 inhabitants there would be 20,805 unregistered mental defectives. It is quite possible that while registered insanity has increased markedly during the last twenty years, with the provision of increased accommodation, unregistered insanity has diminished; in fact, it is well known that the village idiots and the lower grade imbeciles—who were at large all over the country—have accumulated by detention in asylums and now help to swell the registered insane. Two very numerous classes of individuals who should be registered and placed under some control on account of their anti-social conduct are, firstly, the chronic incurable inebriate, dangerous to himself and society and responsible for a considerable portion of the crimes of violence, consequently a perpetual expense and danger to the community; secondly, the imbecile of feeble will-power, slender sagacity, and lack of moral sense. These latter, indeed, form a large proportion of the chronic inebriates who are on the black list. Again, the feeble-minded swell the ranks of criminals and especially are they found among those who are unemployed because unemployable; many imbecile women, not having sufficient intelligence or desire to earn an honest living, lead immoral lives and have numerous illegitimate children. Moreover, the great army of prostitutes in London and our large cities is partly recruited from feeble-minded women. Although feeble-minded persons may be met with in all grades of society, they are especially and for obvious reasons to be found

among the denizens of the one-roomed tenements of our great cities. Unlike the more intense forms of mental deficiency, these defectives are fertile and procreate freely; seeing that "like tends to beget like" it will be a good thing for the race when those who are judged to be unfit for social privileges are registered and segregated in early life. But great care is necessary not to establish any class prejudice; nor must a judgment of fitness and unfitness be determined without careful consideration of each case. I shall, however, have reason to refer to this matter more fully later; suffice it to say that *the increase of registered insanity may be partly explained by a diminution of unregistered insanity; as asylum accommodation has increased, large numbers of this class of patient suffering with incurable mental defect have been admitted and detained for life in asylums; thus helping materially to accumulation, which, as I have already stated, the Commissioners have referred to as an important cause of the increase of registered insanity.*

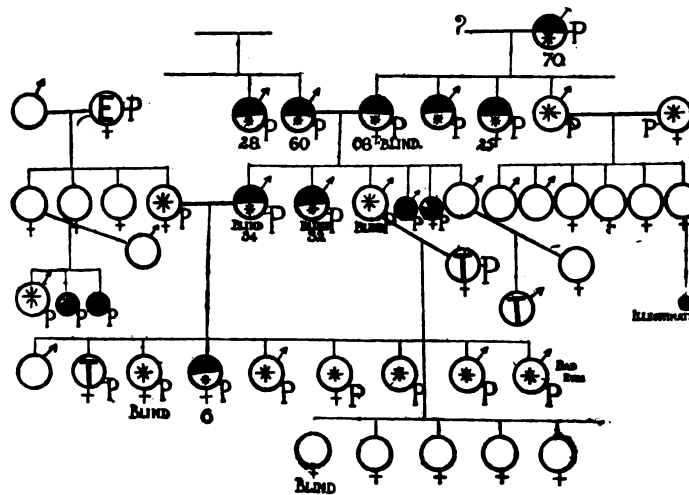


FIGURE 5.

This is a pedigree showing pauperism, insanity, and blindness in four generations (Lidbetter). Half-black circles, Insanity. P*, Pauperism. E, Epilepsy. T, Tuberculosis. Figures denote age at time of attack of insanity.

OTHER CAUSES OF INCREASED REGISTRATION.

Another important cause of the increase is that collective responsibility has replaced family responsibility; and the humane treatment and improved housing of the insane under the control of the people's representatives, with all the legal penalties attached

to any cruelty, have removed the objections the public formerly had to put away an insane relative or friend. Seeing that keeping a lunatic out of an asylum is liable to get both practitioner and friends into trouble with the authorities, it follows that in England certification is the indispensable preliminary to treatment. Certification means incarceration in an asylum. Consequently everything has been tending towards increase of registration and asylum treatment of the insane. Moreover, it has been asserted that certification by the infirmary doctors is encouraged by the payment of a fee for each case; and the numbers transferred from the infirmaries to the asylums under certificate would diminish if the doctors received a fixed salary for this work. Certainly this system of payment does not tend to diminish registered insanity. Nor does the government payment of 4/- to the Guardians for each patient registered; in fact, while not denying that many senile cases are among the most troublesome to deal with and only fit for asylum treatment, yet the facts seem to indicate that a number of aged persons suffering with senile decay, who formerly were unregistered and kept in the infirmary are now certified and sent to asylums. Thus in the Report of the Asylums Committee of the London County Council, 1910, p. 110, it is stated that as many as 4,762 or 23 per cent. of the inmates of the London County Asylums were suffering from dementia, senile and secondary; this indicates clearly that a number of these aged persons who were formerly treated in the infirmaries have helped to swell the registered insane.

OTHER CAUSES OF THE INCREASE OF REGISTERED INSANE BY ACCUMULATION.

Another cause of accumulation has been the steady diminution of discharge of patients as recovered. With the increased housing accommodation the recovery rate has been diminished; this statement is almost paradoxical, but it is the fact that eight years ago, when London accommodation was much more deficient than it is now, it was calculated that 28 per cent. of the recoveries had relapsed within five years and 12 per cent. within one year. In an admirable report of the Clerk of the London County Asylums in 1910, it is stated that out of the large mass of registered lunacy, only 2.39 per cent., according to the medical superintendents, have a favourable prospect of recovery, 5.42 per cent. are doubtful, and as much as 92.19 per cent. are unfavourable.

DECLINING DEATH RATE OF REGISTERED LUNATICS AND ACCUMULATION.

An important cause of the accumulation of the registered insane is that the pauper insane have a prospect of longer life in asylums than they would outside, where they are liable to suffer from the effects of poverty and its consequent insufficiency of food, light, air, warmth and fatal intercurrent or zymotic disease. Again, the death rate in asylums has diminished considerably with the fall in

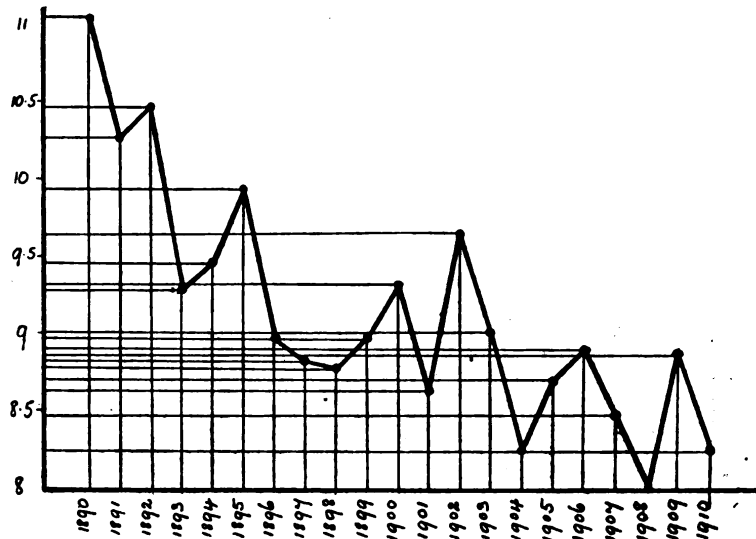


FIGURE 6. Showing percentages of deaths on average daily number of insane on register.

This chart shows the steady fall in the death rate of the L.C.C. Asylums in the last 20 years, from 1890—1910 inclusive.

the death rate outside; also with increased accommodation and improved sanitation of asylums there has been a considerable fall in the death rate from dysentery, tuberculosis, pneumonia, septic and other microbial infective diseases. There is consequently, owing to this declining death rate and diminished discharge rate, a continuous process of silting up with chronic incurable cases of insanity. That this is so is shown by the fact that at the present time nearly one-half of the 20,000 odd inmates of the London County Asylums have been resident in asylums more than ten years. Again, at the end of 1910, no less than 4,238 patients known to have been insane for more than twenty years were in the London Asylums, and in the 1910 report it is stated that such long standing cases have been accumulating during the last four years at rates varying from 125 to 200 per annum.

TABLE I.

The following table, which is made up in four-year periods and is repeated (with the addition of the 1911 figures) from last year's memorandum, illustrates how the recovery and death-rates are continuously declining:—

Period.	Percentage on average number on registers.												F. W. MOTT
	Recoveries.			Deaths.			Recoveries and Deaths.			Combined			
	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.	
Annual Average, 1890—1893	12.29	10.25	11.06	13.48	8.03	10.20	25.77	18.28	21.26				
„ 1894—1897	11.67	10.06	10.71	12.31	7.21	9.27	23.98	17.27	19.98				
„ 1898—1901	8.20	8.10	8.14	10.92	7.58	8.93	19.12	15.68	17.07				
„ 1902—1905	7.72	7.65	7.68	10.88	7.46	8.88	18.60	15.11	16.56				
„ 1906—1909	6.55	6.84	6.72	10.00	7.48	8.56	16.55	14.32	15.28				
Two years, 1910—1911 ...	5.07	5.51	5.32	10.07	6.95	8.29	15.14	12.46	13.61				

HEREDITY AND INSANITY.

In a research by the card system which I have carried out respecting heredity and insanity, I have collected cards referring to 3118 patients who are related or have had relations in the London County Asylums and been discharged or have died. Of these

TABLE II.

Showing Proportion of Deaths and Recoveries amongst "Relative" Cases.

	Discharged.	Transferred.	Died.	Resident.	Total.
Males	260 = 19'0 per cent.	60 = 4'4 per cent.	400 = 29'2 per cent.	647 = 47'3 per cent.	1367
Females	365 = 20'8 per cent.	62 = 3'5 per cent.	399 = 22'7 per cent.	925 = 52'8 per cent.	1751
Total	625 = 20'0 per cent.	122 = 3'9 per cent.	799 = 25'6 per cent.	1572 = 50'4 per cent.	3118

20 per cent. have been discharged, 25'6 per cent. have died, and the remainder 54'4 per cent. still remain in the London County Asylums; and there is a continuous increase in the numbers of related persons resident in our asylums.

I think therefore I have given many and sufficient reasons why the increase of registered insanity does not necessarily mean either an increase of the causes of insanity nor indeed does it reflect a true index of the ratio of insane to sane individuals at the present time as compared with the past. Finally, and in support of this statement, I will refer to a valuable paper by Mr. Noel Humphry, I.S.O., read before the Royal Statistical Society. He affirms from his investigations that there is no proof of the existence of an actual increase in England and Wales, and he concludes on the evidence of several interesting tables drawn from the statistics in the Annual Report of the Lunacy Commissioners, the London Asylums Committee and the Metropolitan Asylums Board, and from the Census returns, that the increase is apparent rather than real for the same reasons that I have given regarding registered London lunacy.

RELATIONSHIP OF PAUPERISM AND REGISTERED LUNACY.

The chart (Fig. 4) given above exhibits the relationship of registered lunacy, pauperism, and population in the County of London; you cannot fail to be struck with the fact that the population has been stationary for twelve years and, naturally, the rapid increase of registered insanity, which is known insanity, causes grave apprehension, nay even alarm, to the layman, and especially the ratepayer; and not knowing the facts which I have

brought to your notice he readily swallows alarmists' statements made in the newspapers by medical men and laymen. Not only does he think of the increasing cost of housing and maintaining the lunatic population, but believing the increase to be very real he naturally asks what are the causes underlying this increase of insanity which goes on in spite of social reforms and he will ask himself, "Is not the eugenicist right in warning us of the dangers of promoting the propagation of the fertile unfit at the expense of the more prudent and consequently relatively less fertile fit?" There is undoubtedly a correlation between the incidence of registered insanity and pauperism. By pauperism I do not mean poverty; for a nation may be poor and the majority of its people may indeed have only a bare subsistence and yet the percentage of insanity may not be high. By pauperism I mean that condition of poverty brought about by the unequal distribution of wealth which is so manifest in our great cities. Here a process of selection takes place whereby those stocks and families with intelligence, energy, and sagacity, who in the past or present time have acquired wealth more or less at the expense of the mentally less favourably endowed form the top layer and more or less grade successively through the professional and middle classes to the smaller tradesmen, artisans, clerks and casual labourers, until finally we come to a sediment of unemployed because unemployable, weak in mind and feeble in body, whether due to inherent deficiency or acquired degeneracy.

REGISTERED INSANITY GREATER IN LONDON THAN IN ENGLAND AND WALES.

A comparison of pauper lunacy and total registered lunacy of England and Wales with London shows, as this chart from *London*

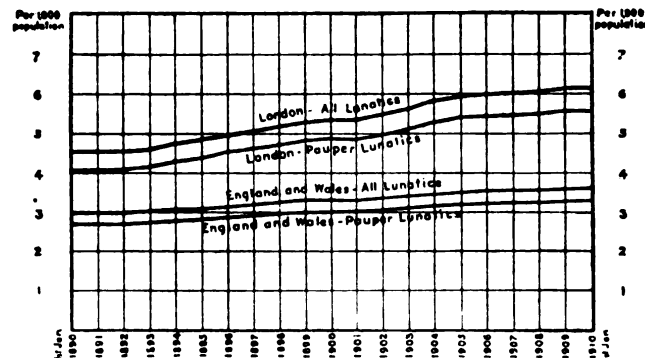


FIGURE 7.

Number of Pauper Lunatics and all Lunatics per 1000 Population on 1st January of each of the years 1890-1910, London and England and Wales compared.

Statistics indicates, a greater proportional increase in London although the population for the last twelve years has been stationary; this may be due to the fact that the housing accommodation for London lunacy has nearly reached its completion; the task will devolve on Greater London in the future.

Another table taken from *London Statistics* shows that relatively to boroughs, cities and towns of England and Wales it will be

TABLE III.

The following table, also taken from volume 21 of *London Statistics*, compares statistics of the pauper lunatics of London on 1st January, 1910, with statistics of several large provincial towns :—

Town.	In county and borough asylums registered hospitals and licensed houses.	In metro- politan district asylums.	Number on 1st January, 1910.				Males.	Total.	Total.	Per 1,000 estimated population
			Number.	In work- houses. Per. centage to total.	Residing with relatives and others.	Females.				
London (Ad- ministrative County)	19,563	6,844	250	9	165	11,966	14,856	26,822	5.5	
Birmingham .	1,669	—	146	8.0	17	930	902	1,832	3.3	
Bradford ...	566	—	201	25.9	10	400	377	777	2.6	
Bristol ...	875	—	538	35.1	122	673	862	1,535	4.1	
Cardiff ...	652	—	25	3.1	118	390	405	795	4.1	
Croydon ...	439	—	34	7.2	1	193	281	474	2.9	
Hull ...	589	—	37	5.7	28	297	357	654	2.4	
Leeds ...	1,115	—	171	12.9	37	669	654	1,323	2.7	
Leicester ...	678	—	58	7.6	28	356	408	764	3.1	
Liverpool ...	2,817	—	356	11.2	19	1,410	1,782	3,192	4.2	
Manchester ...	1,751	—	578	24.7	7	1,137	1,199	2,336	3.6	
Newcastle ...	836	—	2	.2	13	488	363	851	3.0	
Nottingham ..	808	—	206	18.4	103	519	598	1,117	4.2	
Salford ...	668	—	254	27.5	3	501	424	925	3.8	
Sheffield ...	1,018	—	253	18.9	65	650	686	1,336	2.8	
West Ham ...	998	—	32	3.0	25	475	580	1,055	3.3	

From this table it appears that the proportion of lunatics to population in London is unduly large.

observed that although London stands very high as regards numbers in asylums; it has relatively few in workhouses and in their own homes or residing with relatives and others. In London old age pensions, we have seen, have had no influence on asylum admissions, whereas it is known that they have led to numbers of aged persons being kept with relatives and friends outside of London and other large cities where the housing of such senile demented is not likely to be a nuisance to others as it would be in a great city.

There are, however, other reasons which help to make London lunacy higher *pro rata* of the population than that of other cities and boroughs. Mr. John Burns was reported recently to have stated that 70 per cent. of the vagrants of this country are at one time of the year in London. Probably a number of such vagrants are mental defectives or degenerates, and become stranded in the metropolis; moreover, this may happen to lunatics or potential lunatics who come to London looking for work. The pauper population contributes a much larger ratio of lunatics per 10,000 of the population to certified insanity than private cases. This may be partially due to the fact that the friends of private patients are usually desirous and generally able to elude registration altogether in many cases, or at least to postpone it, for shorter or longer periods.

I have thought it would be interesting to ascertain first how the various unions and parishes of London compare as regards the number of lunatics severally chargeable to them, and secondly to compare the same with the admissions from the same unions and parishes during the past two years, as this would give an indication of the extent of present and past lunacy in those unions and parishes. Some remarkable and unexpected results occurred which I have not yet had time to investigate fully in relation to the cause. It will be observed that Happy Hampstead has only a ratio of 3 per 1,000 chargeable to it; whereas London West Central—Bloomsbury, Westminster, and Strand—are the highest. I fully expected that with the disappearance of great blocks of slum property in those parishes, especially the Strand, this high ratio would be found to be due to the effects of accumulation owing to the pauperism of the past, but in the admission ratio per thousand during the two years 1910 and 1911 they easily head the list, especially the Strand. A most remarkable fact is the low admission rate of poor but industrious Bethnal Green. It cannot even be said that it is due to the small numbers of inhabitants relatively to other parishes and unions, for St. George's-in-the-East has a smaller population than the W.C.-district. A reference to that great work of Charles Booth's, "Life and Labour of the People," is of interest in explaining the high rate of pauper lunacy. This would, however, take too long to dwell upon, and I am at present engaged in ascertaining the occupations of those who were admitted from West Central London. It is the centre of pleasure and of vice, of wealth and of degraded destitution. Woolwich is a good

TABLE IV.

STATEMENT showing the ratio per thousand of all pauper lunatics (including imbeciles) chargeable to unions and parishes in the County of London on the 1st January, 1912, to the population in April, 1911, as ascertained by the census.

Parish or Union.	Population, April, 1911.	Total pauper lunatics including imbeciles.	Ratio per 1,000 of population.	
Hampstead	85,510	253	3'0	
Lewisham	174,296	551	3'1	
Wandsworth	479,195	1,946	4'1	
Fulham	153,325	628	4'1	
Paddington	142,576	604	4'2	
Hammersmith	121,603	524	4'3	
Islington	327,423	1,572	4'8	
Woolwich	127,737	628	4'9	
Greenwich	185,688	962	5'2	
St. George's Union ...	117,968	628	5'3	
Camberwell	261,357	1,522	5'8	
Bethnal Green	128,282	754	5'9	
Hackney	273,270	1,635	6'0	
Kensington	172,402	1,033	6'0	
Mean ratio ...	—	—	6'07	
Lambeth	298,126	1,834	6'2	
Poplar	162,449	1,126	6'9	
Mile End Old Town ...	111,375	730	6'6	
St. George-in-the-East .	47,101	316	6'7	
St. Marylebone	118,221	795	6'7	
Chelsea	66,404	462	7'0	
Stepney	53,798	375	7'0	
Bermondsey	125,960	914	7'3	
Shoreditch	111,463	829	7'4	
St. Pancras	218,453	1,874	8'6	
Southwark	191,951	1,735	9'0	
Holborn	112,247	1,114	9'9	
Whitechapel	67,750	685	10'1	
West Central London of Booth County	Westminster	25,451	271	10'6
	Bloomsbury	25,065	265	10'6
	Strand ...	16,858	219	13'0
	County	—	542	—
Total ...	4,503,304	27,326	6'07	

TABLE V.

STATEMENT showing the numbers of lunatics (including imbeciles) admitted to the London County Asylums and the Metropolitan Asylums Board's imbecile asylums during the two years 1910 and 1911, chargeable to the various parishes and unions in the County, with the ratio per thousand to the population of the respective parishes at the census of 1911.

Position on list.

Direct admissions	Total lunatics 1st Jan., 1912	Parish or Union	Population April, 1911.	Direct admissions, 1910 and 1911.			Ratio per 1,000 of population.	
				County	M.A.B.	Total.	Asy.	Total.
1	12	Bethnal Green	128,282	103	22	125	'80	'97
2	2	Lewisham	174,296	181	19	200	1'04	1'15
3	1	Hampstead	85,510	86	17	103	1'01	1'20
4	10	St. George's Union, W.	117,968	125	28	153	1'06	1'29
5	5	Paddington	142,576	175	18	193	1'23	1'35
6	9	Greenwich	185,688	240	22	262	1'29	1'41
7	19	St. Marylebone	118,221	163	13	176	1'38	1'49
8	4	Fulham	153,325	221	12	233	1'44	1'52
9	8	Woolwich	127,737	171	25	196	1'34	1'53
10	18	St. George-in-the-East	47,101	52	20	72	1'10	1'53
11	7	Islington	327,423	388	116	504	1'18	1'54
12	3	Wandsworth	479,195	635	108	743	1'32	1'55
13	23	Shoreditch	111,463	155	23	178	1'39	1'60
14	6	Hammersmith	121,603	177	25	202	1'46	1'66
15	26	Holborn	112,247	160	26	186	1'42	1'66
16	14	Kensington	172,402	257	33	290	1'49	1'68
17	11	Camberwell	261,357	345	98	443	1'32	1'69
—	—	Mean ratio ...	—	—	—	—	1'40	1'73
18	22	Bermondsey	125,960	168	52	220	1'33	1'75
19	20	Chelsea	66,404	100	16	116	1'51	1'75
20	17	Mile End Old Town...	111,375	158	51	209	1'42	1'88
21	13	Hackney	273,270	450	77	527	1'65	1'93
22	21	Stepney	53,798	73	31	104	1'36	1'93
23	15	Lambeth	298,126	423	166	589	1'42	1'98
24	25	Southwark	191,951	327	94	421	1'70	2'19
25	27	Whitechapel	67,750	114	36	150	1'68	2'21
26	16	Poplar	162,449	248	124	372	1'53	2'29
27	24	St. Pancras	218,453	382	166	548	1'75	2'51
28	28	Westminster	25,451	63	2	65	2'48	2'55
29	29	Bloomsbury	25,065	75	28	103	2'99	4'11
30	30	Strand	16,858	73	14	87	4'33	5'16
Totals ...			4,503,304	6,288	1,482	7,770	1'40	1'73

example of a parish in which a large proportion of the population consists of poor but respectable artisans in continuous employment; both its chargeable pauper lunacy and its admission rate stand low as compared with Poplar, Lambeth, and St. Pancras.

CAUSES OF INSANITY.

A person is registered as insane when he is of unsound mind and incapable of taking care of himself or dangerous to himself and others. Now unsoundness of mind may own many causes in varied combinations; practically speaking, they may be divided into inborn tendencies or predispositions and acquired causes the result of environment—in other words, Nature and Nurture: what an individual was born with and what has happened to him since birth. Registered insanity includes not only disordered functions of mind—psychoses and dementia (loss of mind), but all those cases of imperfect development or arrest of development, *viz.*, imbecility and idiocy, due to (1) an inborn, *germinal*, *gametic* and therefore hereditary failure of the higher structures of the organ of mind to develop; (2) acquired, which includes also all those cases due to arrest of growth of the brain from such causes as maternal injuries or disease affecting the developing embryo, therefore *congenital*; also those cases of arrest of development of the brain due to injury of the child from prolonged or difficult labour, as well as cases of arrest of mental development from injury or disease of the brain in early life. From a racial and eugenic point of view the first-named are by far the most important because the defect is germinal and therefore transmissible to the offspring. The lowest grade imbeciles and idiots are often sterile, whereas the higher grade imbeciles as a rule are prolific. Now the crux of segregation of feeble-minded imbeciles, who are not at present registered, is the determination of their fitness for social privileges, and it has to be borne in mind that one important reason why such persons should be segregated is to prevent racial degeneration and racial suicide. It is obvious therefore that the first thing necessary in deciding whether an individual should be allowed social privileges is to determine whether his feeble-mindedness is due to a *germinal defect* or not, and if it is, what is the probability of its being transmitted to offspring. If the clinical evidence is in favour of germinal weak-mindedness and therefore heritable, it is necessary to find out whence came the germinal deficiency. What we want to know is, Did the patient come from good stocks or bad stocks? In a large

family one child may be feeble-minded and all the rest sound, perhaps some may possess brilliant mental characters. We may not be able to ascertain any reason for this child being defective. By the laws of heredity, especially Galton's law of ancestral inheritance, a feeble-minded or insane individual coming from sound stocks of civic worth, is much more likely to breed mentally sound children than a feeble-minded or insane individual of a bad stock in which are found a large number of members exhibiting various forms of degeneracy, *e.g.*, insanity, feeble-mindedness, alcoholism, epilepsy, criminality, pauperism, in fact a general low standard, mental and physical, in stem and branches of the family tree. Vide Figs. 8 and 5.

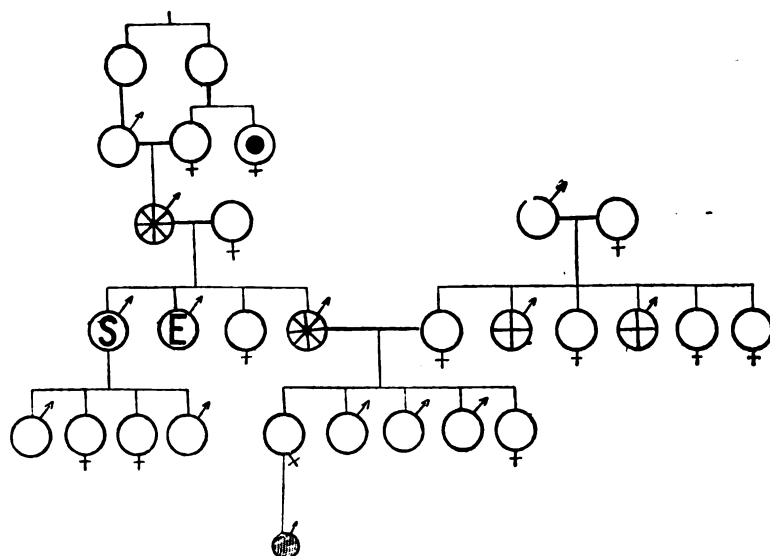


FIGURE 8.

A pedigree illustrating the marriage of first cousins. A genius was the result; he married a healthy woman, and their family consisted of an eldest son, a suicide; a second son, an epileptic; a daughter, healthy, unmarried; and a son, a genius. This man was a genius, but had an extremely well-balanced mind; all his five children are healthy in spite of collateral inheritance on both sides.

Circles with black centre, Physically unsound. Circles in quadrants, Alcoholism. Circles in octants, Genius.

Mental deficiency, whether the defect be germinal or acquired, and due to disease or injury of the developing embryo or child, occurs in all classes of society from the highest to the lowest. But inasmuch as "like tends to beget like" and mental energy and sagacity are all important in the economic struggle for existence,

it follows that the tendency to germinal mental deficiency is most prevalent in the lowest grades of the social scale. Likewise, in respect to mental deficiency due to acquired disease or injury of the developing embryo, the same causes occur in all grades of society; thus as regards congenital syphilis, which is responsible for so much physical and mental deficiency, the lower we sink in the social scale in our investigations, the more are its terrible effects apparent; this is not wholly due to a greater incidence of acquired syphilis in the poor, but to the fact that the disease is more efficiently diagnosed and treated in the better classes. I believe that syphilis is much more prevalent among idle rich men than among the industrious poor. The lower we descend in the social scale, the more however do we find the effects of syphilis among females; and general paralysis of the insane, the essential cause of which is syphilis, becomes more and more common among females; indeed, general paralysis may be regarded as an index of the incidence of acquired syphilis in the population and probably also to some degree a measure of opportunity and efficiency of treatment. Again, the influence of drink, tuberculosis, imperfect nutrition of the mother, upon the developing embryo must play a part in embryonic development of the child. Still the brain in its development is marvellously protected and can call upon all the other tissues of the body to deprive themselves of nutrition, in order that it may grow and develop those innate characters so essential for the preservation of the individual and the species. In fact the brain and the reproductive organs are the master tissues and all others are subservient; thus they are specially protected against malnutrition and from permanent effects of poisonous conditions of the blood unless acted upon for long periods of time.

If insanity is on the increase we should ascertain what are the causes and how they can be prevented. The eugenist would say that it is mainly a question of inheritance and the problem we have to deal with is one of positive and negative eugenics, viz., to promote an increased birth rate of the mentally fit and cut off the lines of inheritance of the mentally unfit. Now an increase of registered insanity would certainly in time tend to diminish the ratio of insane to sane members of the population, because if they are segregated for longer or shorter periods of time, they are in varying degrees prevented from breeding their like.

Facts seem to show that Nature itself is always trying to end or mend a degenerate stock by a signal tendency to the occurrence

of anticipation in successive generations. I have shown this by a study of relatives in the London County Asylums both statistically exhibited by the following figures, curves, and pedigrees.

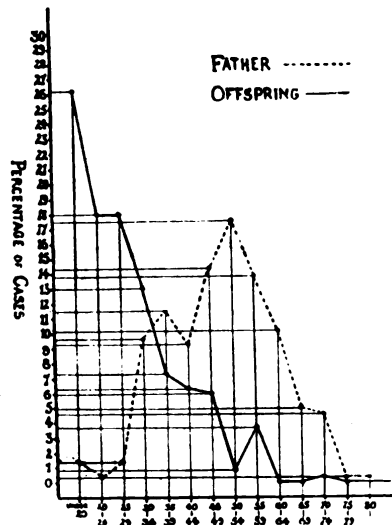


FIGURE 9.

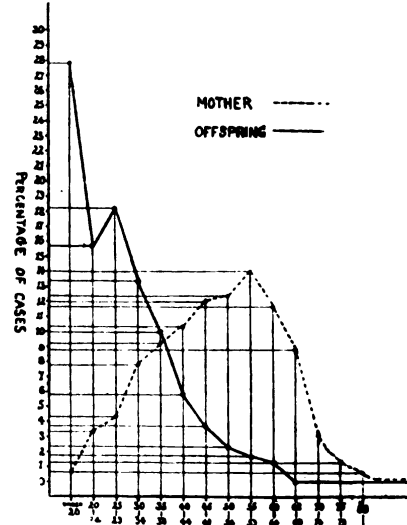


FIGURE 10.

The above figures showing the percentage of cases whose first attack occurred within the given age periods have been compiled from an investigation of the age at the time of first attack in 508 pairs of parent and offspring, from the records of 464 insane parents of 500 insane offspring. The curves clearly show the signal tendency to the occurrence of most of the insanity in the offspring of insane parents at a much earlier age than in the parent, the majority of them being affected before or during the period of adolescence; that is to say, antedating or anticipation is the rule. Nearly 50 per cent. of the insane offspring had their first attack at or before the age of 25, and nearly one-third of these were imbeciles.

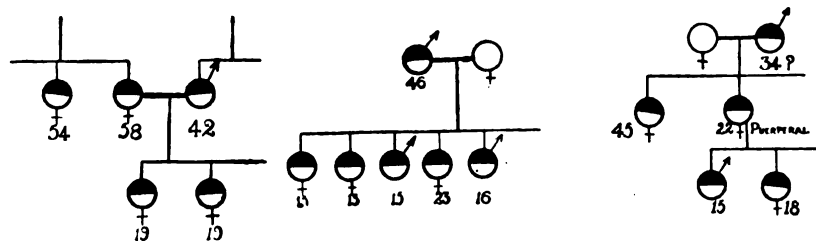


FIGURE 11.

Three pedigrees to illustrate "antedating"; the onset of insanity in the offspring is shown to occur at a much earlier age than in the parents. These pedigrees also illustrate extreme cases of hereditary transmission of the neuropathic taint; as a rule not more than one insane offspring of an insane parent occurs in four or five. The occurrence of insanity in all the children is probably due to the fact that there is a double insane inheritance in all these instances, although it is only shown in one completely, and one partially.

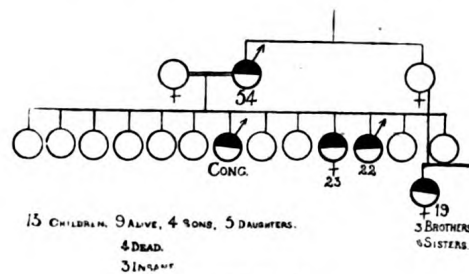


FIGURE 12.

A. B.—, an alien Jew, aged 54 years, was admitted to an asylum for the first time suffering with involuntional melancholia; he has a sister who has not been in an asylum, but, as events turned out, bore the latent seeds of insanity. The man is married to a healthy woman who bore him a large family; the first five are quite healthy, then comes a congenital imbecile epileptic (cong.), then two healthy children, followed by a daughter who becomes insane at twenty-three, then a son insane at twenty-two, and lastly, two children who are up to the present free from any taint. The sister of A. B.— is married, and has a family of ten, seven girls and three boys; one of the females was admitted to the asylum at the age of nineteen, and since this pedigree was constructed a brother of hers has been admitted, aged twenty-four. Half-black circles are insane. This pedigree is instructive; it shows direct and collateral heredity; it also shows remarkably well the signal tendency to the occurrence of insanity at an early age in the children of an insane and potentially insane parent.

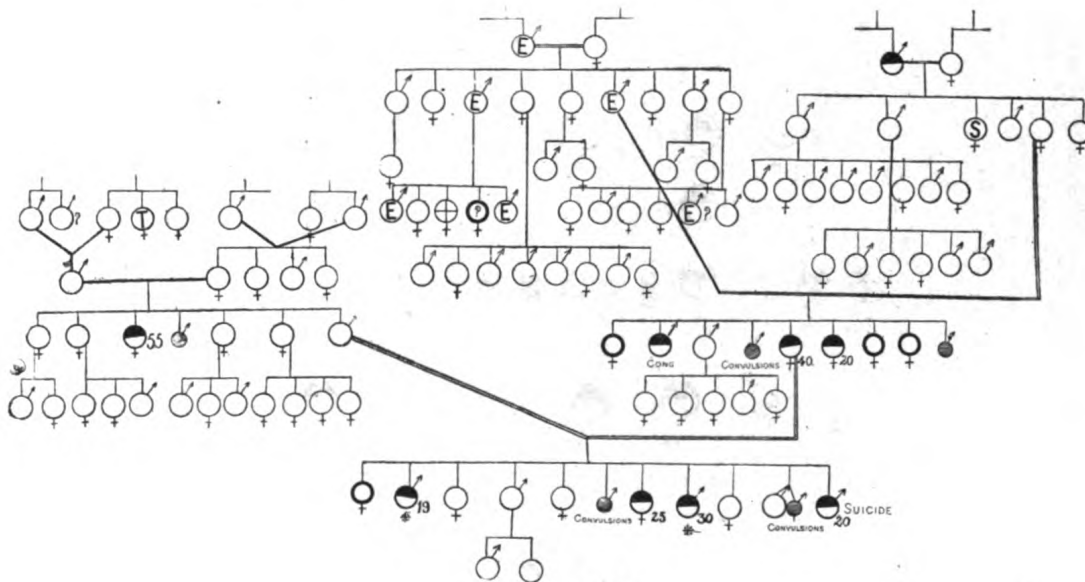


FIGURE 13.

This is a very comprehensive and interesting pedigree obtained for me by Dr. Wilson White, showing the result of marriage of a nearly sound stock in which the temperament was, generally speaking, of the sanguine type; there was only one member insane at fifty-five; she was unmarried;

her four sisters, who were all married, had some healthy grown-up children. The brother himself, perfectly sane and healthy, married a woman descended from stocks in one of which there were many members suffering with epilepsy (E); indeed, her father and her grandfather suffered with it. On the maternal side there was suicide (S) of an aunt and insanity of a grandfather; most of the members of this stock were of a melancholy, brooding temperament. The result of the mating of these two neuropathic stocks is shown. There were nine children, of which three, marked with deep black-rimmed circles, suffered from some form of neurosis, a male congenital imbecile, a healthy male who has five healthy children, a child who died in early life of convulsions, the patient's mother who became insane at the age of forty, a female who became insane at the age of twenty; two females also suffered with some form of neurosis; lastly, a male who died in early infancy. The next generation shows the result of mating this unsound stock with an almost healthy sound stock. There are not as many unsound members as in the last generation, and we observe that the four members that became insane at nineteen, twenty-five, thirty and twenty all had their first attack at a much earlier age than their mother; one of these committed suicide and two were found dead. This pedigree illustrates well the signal tendency to the occurrence of antedating. The sound members of the stock apparently inherited their temperament from the father's side, and the one member that is married has quite healthy children; this looks as if the unsound elements of this degenerate stock had been cleared out by segregation of the unsound germinal determinants, causing intensification of the disease and occurrence of the onset at an early age, thus preventing propagation.

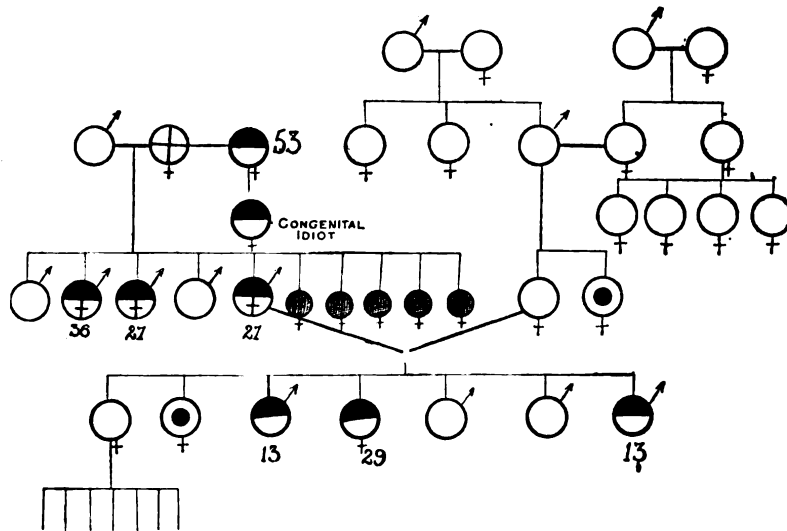


FIGURE 14.

A family of drunken and insane people. The figures with half-black circles are insane; the same with the cross indicates drink and insanity; the circles with only a cross indicate excessive drinking. The two stocks show a marked difference; one side the maternal is practically free from any taint; almost every member of the paternal stock is unsound. The degeneracy commenced with a drunken woman whose sister died,

aged 53 years, in Colney Hatch Asylum, where she had been twenty years; she had a congenital imbecile daughter in Leavesden. The result of mating a sound individual with a drunken woman with insane predisposition is shown in the members of the family born; a son healthy, then two alcoholic sons who were insane at the ages of thirty-six and twenty-seven, then a healthy son, then another alcoholic son, who also was insane at twenty-seven, finally, five daughters who died in early life, probably through the neglect of a drunken mother, indicated by small, shaded, circular figures. One member of this drunken and insane family married into a healthy sound stock. Seven children were the fruit of this marriage; of these, two sons and a daughter were normal, and three were insane, two of them having become insane at the age of thirteen. The clear circle with a black centre indicates bodily disease. I used to give this pedigree as an instance of drink causing insanity, but after the establishment of the card system of relatives I found the notes of the sister of the drunken grandmother; she was an inmate of Colney Hatch for twenty years. It sometimes happens that the one is taken and the other left, and it would have been a benefit to society if the drunken progenitor of this degenerate stock had been taken.

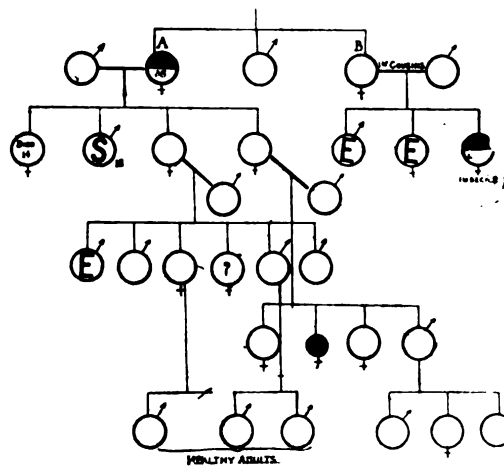


FIGURE 15.

This pedigree shows the result of marriage of first cousins, in both of whom there was a latent neuropathic taint. The family consisted of three individuals, two sisters A and B, and an elder brother, who was married but had no family. B married a first cousin, and although neither of them were insane nor epileptic, yet they had two children epileptic and one a congenital imbecile; this terminated the stock on that side. That there was latent insanity was shown by the result of the marriage and the fact that a sister became insane. A, however, married into a healthy virile stock; she became insane at thirty-eight. Although living many years after she never recovered; the exciting cause was the death of a son by suicide (S) at eighteen. There were two daughters who became mothers of families; the eldest son of one suffered with a masked epilepsy, but no other evidence of neuropathy was shown in this generation. The taint seems to have disappeared, inasmuch as there are healthy, grown-up members of the fourth generation.

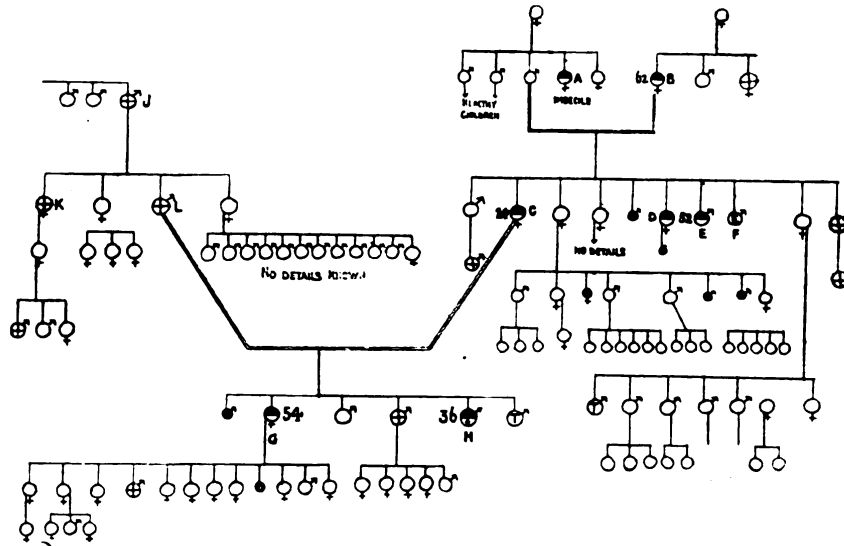


FIGURE 16.

Pedigree showing the apparent elimination of the unsound elements in a stock with dual insane inheritance.

- A. An imbecile but was never put away.
- B. Became insane at the age of 62. Melancholia. In Colney Hatch Asylum for nine months, but eventually died in Caterham Asylum.
- C. Became insane at the age of 24 (St. Luke's Asylum) after the birth of her first child which died in infancy. She was discharged after five months. Her next attack occurred at the age of 38 (when suckling her last child) when she was in Hanwell for twenty months with acute mania. At the age of 43 she was admitted to Colney Hatch and died there seventeen months later.
- D. Very peculiar and eccentric but was never put away. She married twice and by her first husband had one child which died in infancy from convulsions, by her second husband no children. She died between 40 and 50 years. Described by her relatives as insane.
- E. Became insane at the age of 52, acute mania, and died after three days' residence in Hanwell. Had been in feeble health for years and had suffered from lead colic on two occasions.
- F. Epileptic fits from infancy. Admitted to Hanwell Asylum at the age of 28. After seventeen years' residence was transferred to Glamorgan County Asylum.
- G. Became insane at the climacteric period. Admitted to Cane Hill, aged 54 years. Chronic mania. Teetotaler. Her children and grandchildren, with the exception of one son aged 26 who "drinks and bets" are not affected.
- H. Has had delirium tremens. Married an alcoholic now in Islington Infirmary. No children. First certified at the age of 36 and has been in and out of asylums ever since. Has been in Claybury Asylum five times, and other asylums besides. In features he is supposed to resemble his paternal grandfather, but in versatility and humour apparently resembles his maternal grandfather who was a famous clown.
- I. K. I. are reported to be alcoholic, but in spite of this they all lived to good ages. J. died at the age of 78; K. is still living, over 70 years of age; and L. died at the age of 74. Longevity is a characteristic of this stock.

If it be true, then, that Nature is always tending to eliminate degenerate stocks, there must be causes at work both by unsuitable mating and environmental conditions which either tend to revive a latent neuropathic tendency of the stocks or to develop by the cumulative effects of an unfavourable environment the first stage of nervous degeneracy in previously healthy stocks. Morel held that irritable nervous weakness may serve as the starting-point of degeneracy of a stock; according to him it is the source of origin of the neuropathic taint, and I now take the opportunity of saying that the term neuropathic is the expressive word to denote a morbid inheritance in a stock which may manifest itself in different members in different forms. Some members of the stock may be

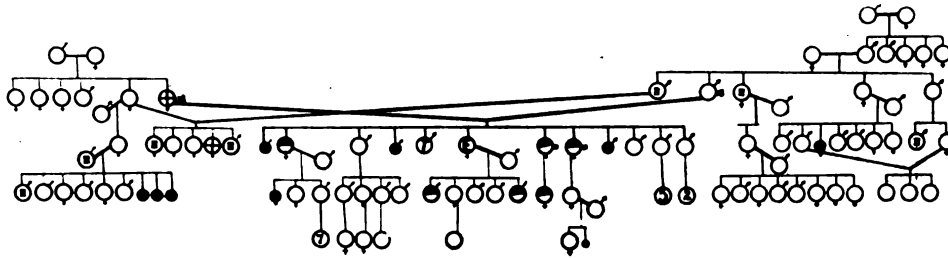


FIGURE 17.

This pedigree is of interest in showing the marriage of two brothers with two sisters. In the first instance the male suffered with heart affection, which was transmitted to the offspring. In the second case the female suffered from cirrhosis of the liver and paraplegia, and was probably alcoholic and syphilitic. The result was three insane and one epileptic offspring. From the first insane daughter the issue was apparently unaffected; but from the next daughter, who had masked epilepsy, of five children born, two were insane. The next two insane daughters each gave birth to an illegitimate child by the same father: one of these children became insane at adolescence, whereas the other has married and has an apparently healthy child. H denotes heart affection. *Half-black circles*, insanity.

eccentric, or of narrow-minded religious beliefs, or visionaries, or suspicious, brooding and melancholic, or unduly mean, selfish and avaricious, or of ungovernable temper and not therefore actually suffering with a disease, but temperamentally abnormal; others may suffer with such nervous diseases as epilepsy in its slight and graver forms, migraine, hysteria, hypochondriasis, neurasthenia, neuralgias, Graves's disease and diabetes. In others the neuropathic tendency may be revealed by alternating depression and optimism or by an inborn lack of moral sense and feeble will-power. The neuropathic inheritance may show itself in criminality and

suicide or the various forms of insanity. Both history and the study of biographies and pedigrees show that insanity and genius are often found in members of the same stock, and even some of the greatest men who have lived have suffered either with epilepsy or insanity. A neuropathic tendency may then suggest a germinal variation, a mutation or departure from the normal average "the honourable ordinary." What has brought it about? Occasionally the commingling of two germ-plasms may bring into association all the qualities necessary for a great genius, as in Goethe's case, told in his own words:—

" Von Vater hab ich die Statur,
Des Lebens ernstes Führen,
Vom Mutterchen die Frohnatur
Und Lust zu fabulieren."

Which, freely translated, means that he derived his energy and physique from his father and his poetic imagination and joyful temperament from his mother.

Again, two germ-plasms which have been long subjected to poisoned conditions of the blood may undergo a pathological mutation affecting only the functions of that most complex and delicate of all organs—the brain. The poisons may be introduced into the body from without for long periods of time as in the case of chronic alcoholism. The poison may be engendered in the body as the result of the growth of parasitic organisms, *e.g.*, syphilis and tuberculosis; or it may be a result of disorder of the functions of one or more of the glands whose internal secretions are essential for vital activities; or glands like the liver and kidneys which are essential for ridding the body of waste products may fail in the performance of their functions. The blood stream no longer under such conditions maintains its normal relation to the organs of the body; a vicious circle tends to occur in which even the specially protected structures may suffer. The brain itself may immediately or quite early feel the influence of the change in the blood, and the unpleasant symptoms aroused may thus be a protective warning to the intelligent mind, and efforts will be made to avoid the danger if the sensibilities are not blunted by habit and tolerance.

Admit that irritable nervous weakness—neurasthenia—may be the starting-point of an unstable nervous condition in a stock which in successive generations may intensify under a continuance of an unfavourable environment; and admit, as we must, that this unstable nervous condition is a special outcome of modern

civilization and does not exist in a primitive people living a simple mode of existence; then as fast as Nature eliminates unsound elements by ending or mending degenerate stocks, social conditions tending to neurasthenia, or nervous weakness as the term implies, may be produced by a vast number of combinations owning a social cause related to unphysiological modes of existence causing bodily and mental stress. Among the most important are prolonged poisoning of the body including the specially protected structures, the brain and the germ cells, by indulgence in excess of alcohol, syphilis, tubercle, lead, and the drug habits; the nervous exhaustion caused by the poisons of infectious diseases, fever and bodily diseases and the anxiety and mental pain associated therewith. The nervous exhaustion resulting from sexual excesses of all kinds, and from the mental pains arising from the ungratified natural desires of the sexual passion, from the stress of city and town life with its feverish pursuit of gain and pleasure, from competition whether in examination, occupation or business, from the constantly increasing departure from physiological modes of life. The existence of more refined physical and mental enjoyments bringing with them desires and emotions previously hardly known or realised; marriage without parentage and restriction of the birth of offspring, starving the maternal instinct in which is rooted the highest altruistic feelings, developing the neurotic self-regarding temperament which so frequently precedes hysteria and insanity. Then prolonged emotional stress, *e.g.*, grief, especially the grief that "does not speak but whispers the o'er fraught heart to break"—and hatred which rankles in the breast; sudden emotional shocks, *e.g.*, disappointment in love, loss of a dear one, and, too often among the poor, death of the bread-winner and breaking up of the home, are the exciting causes of a mental breakdown. All these depressing conditions acting on the mind produce an injurious reaction in the body, causing sleeplessness, loss of appetite, and failure of the digestive and assimilative processes. Restoration of nerve potential and the nutrition of the whole body may thus become impaired, and a vicious circle produced which by continuous expansion tends to disturb more and more the biochemical equilibrium of the body functions leading to the generation of chemical poisons in the body or to failure of the excretory organs to eliminate poisons which should be cast out of the body. This auto-intoxication reacts upon the sensitive and exhausted brain, causing further mental depression (melancholia) or by paralysing highest control to uncontrollable agitation and

excitement (mania). It is obvious therefore that sociological conditions play an important part in the production of insanity; moreover, it shows that certain occupations or no occupation, may predispose to insanity. Nevertheless, nothing to my mind proves the influence of the inborn predisposition more conclusively than the fact that there are individuals born of stocks mentally and physically sound in whom no acquired conditions, *e.g.*, disease, drink, poisons, engendered within the body or taken from without, head injuries, emotional shock, distress, and even profound misery and destitution combined, can render insane. There are others, and these are in most cases derived from a neuropathic stock whose mental equilibrium may be disturbed by any one of these conditions or even without any apparent cause except the physiological conditions appertaining to the functions of the sexual glands at puberty and during adolescence, the puerperium, lactation, and the climacteric period in women. Between these two extremes are all gradations of mentality, from the congenital imbecile, the epileptic, and the insane adolescent dement at one end of the scale, to the potential sound mind and body, that no combination of acquired conditions can render permanently insane.

PRACTICAL PROBLEMS.

A great step forward has been made by the discovery of the micro-organism of syphilis; it is now widely recognised that this is the essential cause of the most terrible form of mental disease—general paralysis of the insane. It is possible that early and more efficient treatment by new remedies, together with a blood test, recently introduced, may have a pronounced effect in reducing the numbers of this form of insanity. In the preface to the third volume of the *Archives of Neurology* issued from the Pathological Laboratory of the London County Asylums in 1907, after calling attention to the importance of the study of the causes of insanity before we can hope to treat it, I made the following quotation from an American writer on Psychiatry:—

“Fortunate would be the community in which there was a fully equipped and well-organised psychiatric clinic under the control of a university and dedicated to the solution of such problems. The mere existence of such an institution would indicate that people were as much interested in endeavouring to increase the public sanity as they are in the results of exploration in the uttermost parts of the earth, or in the discovery of a new star.”

Shortly after this was published, Dr. Henry Maudsley, a man whose experience and philosophical works on Mind and its Pathology have long entitled him to the foremost place among British alienist-physicians, called upon me and made the offer to give the London County Council £30,000 if they would build a hospital for acute mental diseases with a pathological department for scientific research. There were many difficulties, and at last after four years have lapsed the site has been found and the plans have passed the Commissioners.

In Volume IV of the *Archives*, Dr. Maudsley wrote for me a paper entitled "A mental hospital, its aims and uses." Nothing that I could say can add to the arguments he uses nor so infallibly demonstrate the genuineness of the conviction of this great man, of the necessity of such a hospital as the fact that he was willing during his life to give a large part of his fortune for the purpose. I only hope and trust that he may live to see it, not only built, but in active operation.

The general public should recognise, as they have done in America, the great importance of the study of insanity in its earliest and most curable stage, and the necessity of focussing scientific inquiry and research on mental disease if the physician is no longer to remain satisfied that he cannot minister to a mind diseased. But he can best learn to minister to a mind diseased and to prevent insanity by a study of each case as a biological and sociological problem, in which a neuropathic inheritance combined with disordered functions of the body, due to poisons engendered within or introduced from without, conspire together in varied degrees to derange the mind.

F. W. MOTT.

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Microscopical Investigation of the Nervous System in Three Cases of Spontaneous Myxœdema.¹

By R. BRUN,² M.D., and F. W. MOTT, M.D., F.R.S.

IN spite of the increased interest now taken in the pathology of the thyroid gland, the literature on the microscopical condition of the nervous system in the various forms of hypothyroidism (cretinism, cachexia thyropriva (Kocher), and spontaneous myxœdema) is extremely limited. Although certain alterations, of a general character, in the nerve-centres of thyroidectomized animals have been recorded,³ no systematic investigation has been published on changes occurring in the human subject dying of myxœdema. In a report on the "Cerebral Lesions in Psychoses of Toxic Origin," presented to the Fifteenth International Congress of Medicine, at Lisbon, 1906,⁴ one of us (F. W. M.) described the chromatolytic changes of the cortical cells in one of the three now recorded cases of myxœdema; he also observed the marked change in the cells of the medulla oblongata, and for this reason he was induced to seize the opportunity when the occasion arrived of obtaining further material for microscopic examination, as one case did not seem to be sufficient for a definite statement

¹ From the Pathological Laboratory, London County Asylums, Claybury.

² Assistent am Hirnanatom. Institut u. an den Nervenpoliklinik der Universität in Zürich (Professor C. v. Monakow).

³ W. Edmunds, "The Changes in the Central Nervous System resulting from Thyro-parathyroidectomy," *Proc. Roy. Soc. Med.*, 1912, v (Neur. Sect.), pp. 179-195.

⁴ *Congrès internat. de Med.* (XV, Lisbonne), 1907, Sect. VII, fasc. 1, pp. 111, ff.

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to be made. We are unable to find any further reference to this subject in the neurological literature of the last twelve years. We hope, therefore, that the following record of three cases, all of which died of certain grave symptoms, due, in all probability, to anatomical changes in the autonomous bulbo-motor system, will be of some interest. Unfortunately one of the three cases could only be very incompletely investigated, but owing to the fact that by its clinical aspect it completes in some respects the other two, we felt justified in including it.

CASE I.

(1) *Clinical Notes.*

S. C., aged 52, married, was admitted to Charing Cross Hospital on April 17, 1902, under Dr. F. W. Mott.

Previous history: The parents of the patient died of unknown diseases. There were sixteen children in the family; of these only one brother and two sisters (including patient) were still alive. Patient herself has had eight children, three of whom are still alive; three died early, between $1\frac{1}{2}$ and 2 years of age, one died two days after birth and the last one was stillborn. Shortly afterwards, at the age of 45, the patient ceased to menstruate; previously she had always been regular. At the time of the menopause and since, the patient had been under treatment for anæmia; she also complained at the time of some pains in the joints, especially the elbows. Four years before admission she used to attend the out-patient department at the Charing Cross Hospital, under the care of Dr. Mott, for typical symptoms of myxædema. Thyroid "tabloids" were prescribed and she improved greatly under treatment; she attended regularly for about fifteen months, but after that time (during the last three years) she has not been to the hospital, nor has she taken "tabloids" regularly; but only occasionally until the stock which was given to her had been used up. Just before Christmas, 1900, she seems to have had a sort of fit, falling unconscious off a chair. There was no recurrence of the fits, but she has often felt giddy since, and she says that when walking she has a sensation as if she would fall backwards, so that she did not dare to go out without another person accompanying her. She also felt very weak. Her condition becoming serious she again came to see Dr. Mott at the Hospital, on account of œdema and pain in the ankles, both having persisted now

more or less for nearly a year, the œdema, however, coming on in the evenings only. She also complained of breathlessness, giddiness, and drowsiness during the day, and of sleeping very badly; and for these symptoms she was admitted.

Present state: Patient is a cachectic and very anæmic-looking woman of pale yellowish, almost waxy complexion. The skin is dry and thickened, especially over the arms and hands, the latter being increased in size. There is also dryness of the hair, which does not fall out, however. The face is not much swollen, but shows some puffiness under the eyes. The condition of teeth fairly good. There is some œdema of the ankles. The first sound of the heart is very weak, otherwise nothing noteworthy. The pulse is 80 and weak; the morning temperature is 97° F. Hæmoglobin, 55 per cent.; urine clear, pale, acid; specific gravity 1015. No albumin. The speech is slow and monotonous. The intellect seems to be generally dull and enfeebled, and there is a slowness of thought as well as of expression, but sometimes her mind seems bright.

She was placed upon thyroid tablets, but without any improvement occurring.

April 30: The patient has been very unwell to-day; complained of pains in the abdomen and has been sick. The evening temperature is 100·4° F., pulse 108.

May 1: She is very drowsy and apathetic and speaks very little; she also vomited or spat out every nutriment as soon as she had taken it. (Paralysis of swallowing?) The pulse has risen to 136, the heart beating very feebly. No clinical signs discovered in the lungs. Respirations 24; temperature 98·2° F. There appears to be tenderness over the chest, but no objective signs of abdominal disease, and only with difficulty can she be induced to indicate pain in her abdomen.

On May 2 and 3 the condition was about the same, there was still marked tachycardia (112 to 144 in the evening), and impossibility of swallowing; the respiration rate was between 24 and 28. She did not recognize her relations who visited her. Nutrient enemata were administered but not retained.

May 4: In the morning the patient seemed somewhat better, which may be attributed to the successful employment of a drip enema in the night. She was able to take some nutriment by mouth and spoke to her husband. The pulse, however, remained still very frequent 128 to 136. In the evening she suddenly collapsed and died.

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(2) *Autopsy (May 5, 1902).*

Body poorly nourished. No œdema. Brain: Convolutions normal. In the choroid plexus of the lateral ventricles are several small whitish thickenings. Pituitary body very small. Unfortunately this was not preserved for examination. Thyroid: On removal of the larynx and trachea there is an obvious atrophy of both the lateral lobes and isthmus. In what remains of the right lateral lobe is a small yellowish nodule, $\frac{1}{4}$ in. in size, the greater part of the atrophied gland appears to be fibrous in character, the caseous nodule has the appearance of a tubercle or gumma. Lungs very small, atrophied; no evidence of pneumonia, pleurisy, or tubercle. Heart very small; nothing noteworthy except a slight atheroma of the anterior mitral cusp. Kidneys, 3 oz. each; atrophied; capsule not adherent, though the surface is slightly granular, and there are one or two small cysts. Spleen, 4 oz.; liver, 2 lb. 2 oz., nothing noteworthy; gall-bladder normal. Uterus very thin-walled; the muscle appears degenerated, showing whitish specks and striæ. Ovaries very atrophied (size of a small bean). Apparently there was excessive involution of the reproductive organs. The larynx and trachea with the atrophied thyroid was preserved as a museum preparation. Portions of the brain and medulla were taken by Dr. Mott for examination. These were embedded in paraffin after hardening in 5 per cent. formol and subsequently in alcohol.

(3) *Microscopical Examination.*

(a) *Thyroid.*—A small piece of the atrophied right lateral lobe was cut out of the museum preparation, embedded in paraffin and sections prepared; these were stained with hæmatoxylin and eosin, and with Van Gieson's method (fig. 1). On examining these we were astonished to find the glandular tissue comparatively well preserved, the acini only being of somewhat irregular form and size, but containing plenty of apparently normal colloidal substance. The fibrous tissue, however, is markedly increased and many of the acini are atrophied. There is a marked increase of lymphoid tissue.

(b) *Nervous System.*—The various pieces of the brain and medulla oblongata embedded in paraffin after a few days' fixation have been cut with the Cambridge rocking microtome. The sections were stained with polychrome methylene blue and by Nissl's method. The pieces of cortex

were from the frontal and occipital lobes, and the chromatolysis observed had already been described by one of us (F. W. Mott) in toxic psychoses.

*Detailed Account of Microscopical Changes, especially of the
Medulla Oblongata.*

Nervous System.—(1) Frontal cortex: A large number of the small and middle-sized pyramidal cells exhibit a slight degree of com-

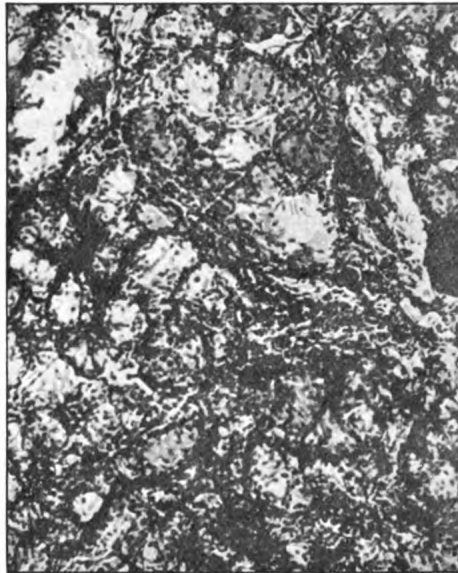


FIG. 1.

Photomicrograph of a section of the thyroid gland from Case 1.
(Magnification 140.)

mencing chromatolysis; many of the cells show a more advanced histological change, for the nuclei are eccentric and the Nissl granules are disintegrated into a fine dust or small mass with crumbling edges, but there is little evidence of swelling of the cells. (2) Occipital cortex (calcarine): In the intergranular layer of Vicq D'Azyr a great number of the polygonal, star-like cells show marked chromatolysis; most of them exhibit nuclear eccentricity. (3) Medulla oblongata: Most of the bulbar nuclei are more or less affected, but it can be easily seen that the degree of change shown by different nuclei is very variable in intensity.

EXPLANATION OF PLATE.

- (1) Cell groups from the nucleus ambiguus vagi, showing terminal chromatolysis: (a) Case I, (b) Case III.
 - (2) Group of cells from the nucleus gelatinosus of the solitary tract (descending ninth root). Case III, advanced chromatolysis.
 - (3) Group of cells from the nucleus hypoglossi, Case III, showing first degrees of chromatolysis.
 - (4) Chromatolytic cells of a sympathetic ganglion of the lumbar plexus, Case III.
 - (5) Nucleus dorsalis vagi, Case I. All cells show advanced chromatolysis.
 - (6) Anterior horn cells of the dorsal cord, Case III. Advanced chromatolysis.
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BRUN and MOTT: *The Nervous System in Spontaneous Myxœdema.*

Whilst the big motor cells of the spinal accessory and hypoglossal nuclei show only a certain degree of poverty of chromatin substance, but no advanced chromatolytic changes, the groups of cells belonging to the vagus system are, without exception, in a most obvious and advanced stage of chromatolysis. In the dorsal vagus nuclei (Plate—5), most of the cells are markedly changed, a number of them showing nuclear eccentricity and a very advanced disappearance of basophile staining substance of the whole cell except at its periphery. There are also seen many shrunken, deeply stained forms without any distinct structure (vide Plate—5) being distinguishable. In the nucleus ambiguus vagi (caudal half) nearly all the cells exhibit total chromatolysis with nuclear eccentricity (Plate—1, a). The other association nuclei of the formatio reticularis are in various degrees but less affected. Next to the vagus nuclei the gravest changes are seen in the nuclei of the posterior columns, a number of the principal cells of both Goll's and Burdach's nuclei showing a certain amount of chromatolysis and peripheric nuclei; a few also appear slightly swollen. The big, marginal cells belonging to the nucleus gelatinosus of the descending fifth root are all more or less affected. Among the cells of the olives a considerable number are seen exhibiting chromatolysis, all cells showing an increase of yellow pigment.

(4) *Résumé and Conclusions.*

The history of the last five children being either stillborn or feeble suggests the possibility of a syphilitic infection. Shortly after the cessation of menstruation this woman developed gradually the syndrome of myxœdema. For fifteen months she took regularly thyroid tablets and the symptoms greatly improved. She then neglected the treatment, and did not reappear at the hospital until a severe cachexia had supervened with all the typical symptoms of myxœdema. Shortly after admission into the hospital there was a sudden aggravation of her morbid condition with obvious symptoms of acute bulbar vagal paralysis—viz., persistent tachycardia, difficulty of swallowing and of speech, accompanied by psychic disorientation (she did not recognize her relations). On the fourth day after the attack she succumbed.

Although in the case-book the impossibility of taking food by mouth is not especially denoted as a paralysis of deglutition, we have every reason to believe it really was one. First of all, the description of the condition in the clinical notes saying that the patient seemed to vomit

or "to spit out every bit of food as soon as she had taken it," then this condition being so closely associated with a persistent tachycardia and, finally, the complete absence of any anatomical change in the gastrointestinal tract found post mortem to account for these symptoms. The transitory recovery of swallowing shortly before death is not to be wondered at if we remember that quite a similar tendency towards an early re-establishment of those vital functions has often been observed similarly in many cases of acute bulbar paralysis due to thrombotic softening in the medulla. For the same reasons, we are also partly inclined to associate difficulty of speech with a suspected vagal paralysis; for even the most advanced cachexia or the most serious weakness does not, as a rule, prevent speech. This functional failure of the vagus system, although arising almost suddenly, was not altogether without prodromal symptoms, for it was noted that the heart sounds were weak and the pulse feeble on admission.

The cell changes found in the cortex and the medulla are such as correspond to a general sub-chronic intoxication: Chromatolysis of very various degrees, even in the same nucleus, without much swelling and not always followed by nuclear eccentricity. It will be noticed, however, that in the medulla the different nuclei are affected in varying degrees of intensity. The twelfth nucleus, for example, showing very little change, whereas both the dorsal and the ventral vagus nucleus are throughout affected in a most serious manner. This, again, corresponds very well with the terminal clinical stage of a fatal vagal paralysis such as was presented by our patient during the last four days of life.

As for the cortical changes, we will not go so far as to correlate these with any special functional disturbance or symptom manifested during life, except it be the slowness of speech and ideation characteristic of the disease; nor can we do more than suggest that the chromatolysis of the stellate cells of the visual cortex may be correlated with the disorientation and non-recognition of her friends during the last four days of her life.

Among the changes of the other bodily organs, the excessive atrophy of both ovaries deserves a more than passing consideration, for it is a well-known fact that myxœdema is especially liable to occur in women after the cessation of the sexual functions. Four cases have been reported by Saltier¹: In two of these the symptoms followed a curetting,

¹ Saltier, "Four Cases of Myxœdema," *Australas. Med. Gaz.*, Sydney, 1911, **xxx**, p. 441.

and in one an oöphorectomy. Again, the statistics of hypothyroidea collected by A. R. Elliott¹ show that most of the cases occur in women, the proportion being seven females to one male ; moreover, the majority of female cases commence at the climacteric period.

CASE II.

(1) *Clinical Notes.*

C. O., aged 56, was admitted to Charing Cross Hospital on April 29, 1906, for a strangulated umbilical hernia. The patient had suffered from myxœdema for about three years, for which, presumably, she had been treated. Two years before admission she acquired an umbilical hernia which became incarcerated on April 27, 1906, at 10 a.m.; she had then severe pains in the abdomen and during the day vomited, food first, bile later. Since then pain was continuous, but she did not vomit again. There was absolute constipation.

Present state: The patient is a stout woman of a general puffy and pallid appearance. Pulse 82, regular, of good tension; temperature sub-normal, 96·8° F.; urine acid, containing no albumin. There is a swelling in the umbilical region with a very tense, red, inflamed centre, obviously due to a strangulated hernia.

April 29, 1906: The operation was at once carried out by Mr. F. Wallis under chloroform-ether anæsthesia and offered nothing of peculiar interest. During the following night the patient slept well and had only a very slight vomiting of a little mucus; the temperature was normal, the pulse good.

May 6: Dressed. The wound has healed by first intention.

May 9: The patient is getting *non compos mentis*; she is very restless. Pulse slow, 60; respirations 16 to 18.

May 11: Mental condition much worse; she is noisy and restless, singing aloud songs and psalms.

May 12: Pulse still very slow, 54 to 62; temperature 96·4° F. Thyroid extract administered.

May 16: The mental condition remained the same. Pulse very much weaker, but still slow (64). The patient sank gradually and died.

¹ A. R. Elliott, "Incomplete Myxedema," *Journ. Amer. Med. Assoc.*, Chicago, 1908, L, p. 1763.

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(2) *Autopsy (Twenty-six Hours after Death).*

A somewhat stout woman, body well nourished. Abdominal scar, 3 in. in length, healed by first intention. Rigor mortis present. Skull of normal thickness. Dura not adherent, normal. No escape of subdural fluid. Pia arachnoid a little congested but showing neither opalescence nor thickening. Brain: Weight 2 lb. 8 oz.; each hemisphere 1 lb. 2 oz.; cerebellum and brain stem together 5 oz. Convolutional pattern complex. Brain substance very œdematous. Ventricles not dilated. Convolutions neither flattened nor atrophic; ependyma not granular. On the under surface of the right lateral cerebellar lobe there is an irregular-shaped fossa, about as large as half a small walnut, with a thin pia arachnoid membrane; it has the appearance of an old atrophic process, the cause of which is not discoverable. Larynx and trachea normal; bronchial glands enlarged and pigmented. Thyroid: Lateral lobes small, isthmus atrophied; consistence appears normal, and upon section there is no obvious naked-eye change. Lungs slightly congested, the left showing slight œdema of the base. Heart, 9 oz.; endocardium slightly opaque; cardiac muscle soft; slight atheroma around the aorta. Omentum, some small intestines and transverse colon slightly adherent to the abdominal surface of the wound; no pus. Liver, 2 lb. 10 oz.; apparently normal; the gall-bladder contains four gall-stones. Spleen, 5 oz.; soft, normal. Kidneys, 4 oz. each, both normal. Transverse colon: A large mass of omentum is adherent; inflammatory changes present. Intestine: Nothing abnormal. Uterus: Nothing abnormal. Neither of us saw the patient during life. The brain was obtained by one of us (F. W. M).

(3) *Microscopical Examination.*

Material: (1) Some preparations from the thyroid gland stained with hæmatoxylin-eosin and with polychrome methylene blue. (2) Paraffin blocks of small pieces of the liver, spleen, heart, and kidney. (3) One paraffin block of the spinal cord (four different levels); some preparations of the ascending frontal and parietal convolutions.

The brain, unfortunately, having been thrown away, the condition of the medulla oblongata was not examined in this case.

(a) *Organs.*—The thyroid (fig. 2): Sections of the gland stained with hæmatoxylin and eosin exhibit a considerable amount of colloid sub-

stance, but the epithelial cells of the acini are very small and atrophied, most of them showing nothing more than the nucleus. Again, numbers of atrophic acini without a lumen can be seen, those consisting simply of a crowd of atrophied cells huddled together. There is also throughout the sections of the gland a very considerable increase of connective tissue and here and there small accumulations of lymphocytes are to be seen. Kidney (Van Gieson's stain): In some places the epithelial cells of the convoluted tubules appear to be swollen up and as if about to undergo desquamation, many lumina being filled with crumbling masses

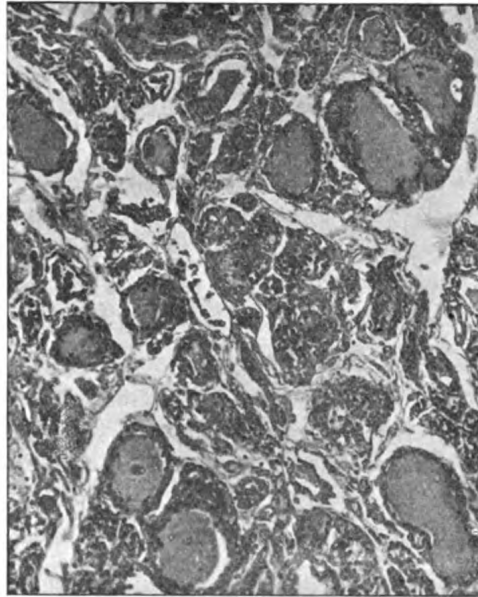


FIG. 2.

Photomicrograph of section of the thyroid gland, Case II. (Magnification 140.)

of coagulated exudation. Some arteries show their walls considerably thickened, this thickening being confined to the media and adventitia. The liver shows some increase of connective tissue surrounding the gall-ducts and veins, and some round cell infiltration of the adventitia of many arteries. The parenchyma itself seems to be intact. In the spleen nearly all the arteries show an intense endarteritis obliterans, numbers of the lumina being filled up. Heart: There is also marked endarteritis of most of the arteries of the heart; the muscle-fibres contain a great amount of brown pigment.

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(b) *Nervous System*.—Anterior central convolutions: The Betz cells of the motor area do not reveal, on an average, any coarse change; yet they are not so rich in chromatin as usual, and some are even in the first stage of chromatolysis. Very few of them exhibit any evidence of advanced chromatolysis. In the sections through the posterior central convolutions no obvious changes can be seen. Spinal cord: The motor cells of the anterior horns are generally quite intact, showing well the Nissl granules, but occasionally here and there one isolated cell can be seen with commencing or even advanced chromatolysis.

(4) *Résumé and Conclusions from Case II.*

A woman, aged 56, and suffering for three years from myxodema (which in all probability came on about the climacteric) has an umbilical hernia which becomes strangulated and leads to an operation. The wound heals up, and all is apparently going well until the tenth day after the operation, when an acute psychosis breaks out, with symptoms pointing to an acute mania, and accompanied by a marked slowness of the pulse which contrasts strangely with the patient's intense motor excitement. This condition persists a few days and in that short space of time leads to a fatal issue.

We have but little doubt that in this case the symptom of slowing of the heart, in spite of the motor restlessness and excitement, strongly indicates a functional disturbance of the vagus centres in the medulla, that is to say, with a state of continuous excitement of the cardiotonic vagus nucleus, a condition which probably later on led to a sudden failure or paralysis by exhaustion, causing death. We do not know whether there is a distinct connexion between this medullary condition and the psychosis or not; it may be that the latter was started by the disease of the bulbar centres or vice versa. In any case it is unfortunate that the medulla oblongata was not preserved, for it is probable that we should have found changes in the vagus nuclei, possibly of a similar character to those in the first case, but not so marked.

The arterial disease found in several of the internal organs seems suspicious of syphilitic infection.¹

¹ This coincidence of disease with myxædema has been noticed by two French authors, Roussy and Chatelin.

CASE III.

(1) *Clinical Notes.*

M. McC., aged 37; occupation formerly a servant. Admission to Claybury Asylum on October 16, 1912.

No family history could be obtained, nor much of her previous life, beyond the fact that she had been in bad health for some years, and had been frequently treated for anæmia and "nerves," undergoing, among other courses of treatment, the Weir-Mitchell cure. Ten days before admission she started with a sudden attack of melancholia without obvious cause, and accompanied by vivid visual hallucinations. She spoke incoherently, weeping aloud and clasping her hands, even doing this among people in the streets; this led to the attention of the police, by whom she was taken to the infirmary and subsequently transferred to the asylum.

State on admission: A rather stoutly built woman of somewhat pasty and pale complexion. She seems very anæmic and in bad general condition of health. She was seen by one of us (F. W. Mott) a few days after admission, and the following observations were made: (Edema of the eyelids, skin and hair very dry, suggesting myxœdema. She replied to questions in a slow and wearied manner with a Scotch accent, but at the time she was seen in the laboratory she exhibited no marked mental disturbance, and it was decided that she was a case of myxœdema. A report to that effect was made to Dr. Jones, who was kind enough to send the case for diagnosis. It appeared to be the opinion of Dr. Jones that the patient was suffering with myxœdema.

The following are the notes from the case-book: Tongue foul, no teeth on the upper jaw, the other teeth are carious. Heart and lungs normal; the pulse, however, is rather slow. Urine acid, 1030 specific gravity, containing much urates and some albumin (one-sixteenth of Esbach's tube), but no casts. Nervous system: Pupils equal, reacting to both light and accommodation. There is marked slowness of speech. Knee-jerks exaggerated. Mental condition: The patient is very restless, refusing to stay in bed and to keep any clothes on. She does not know where she is nor how she got here, and talks incoherently about "God's good man," and the "lights of heaven," and says that to-morrow the world would come to an end and that nobody could help her. She gives a very rambling account of her previous life, saying that her memory

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is bad. She seems to be very depressed. Therapy: 5 gr. of thyroid extract three times a day.

October 23: The patient is still very depressed, thinks that she has no friends, that she is beyond ever getting well, that she is a confirmed invalid, and a burden to her family. She shows some inclination to be ecstatic, hears the voice of God, and strips herself to pray. At night she is very restless and has to be closely watched.

October 25: Examination of the blood. It contains about 4 million erythrocytes and 12,000 leucocytes, most of them polymorphonuclears. Therefore there is no evidence of a grave anæmia, but marked leucocytosis.

October 26: The patient is becoming much weaker and is unable to swallow properly. The temperature is subnormal, 95° F., and the pulse extremely slow, never rising above 48.

October 27: There is complete inability to swallow. Nutrient enemata are not retained, but she is able to retain normal saline enemata.

October 28: The patient has remained in a semi-soporose condition, and has vomited some dark-coloured vomit. She died in the night.

(2) *Autopsy (Eleven Hours after Death).*

A stout woman with physique slightly above average and good muscular development. Teeth carious. Pupils equal, 3 mm. Dura mater *nil*. The subdural and also the subarachnoid space contain some excess of clear fluid. Pia arachnoid very little thickened, stripping readily. Sinus and vessels *nil*. Weight of the brain, 1,230 grm., each hemisphere 530 grm. (510 grm. after stripping), brain stem and cerebellum together weigh 150 grm. Brain of average convolutional pattern, showing no deformity. Some slight frontal and prefrontal wasting; no softening. The pituitary body is somewhat enlarged, causing the gland to bulge slightly over the border of the posterior clinoid processes. The bone is not eroded. The enlargement seems to be confined to the glandular portion. The thyroid is, perhaps, rather smaller in size than usual; it is pale in colour, and on section appears to be densely fibrous in parts, and shows no colloid. A small parathyroid is attached to it. Right lung free, left lung adherent along its posterior surface. Bronchi catarrhal and filled with grumous, blood-stained, viscid fluid. Both lungs broncho-pneumonic and exhibited a

commencing gangrenous patch. No visible tubercles. Pericardium free. Heart, 260 grm., atheroma, muscular substance of normal appearance. Liver, 1,570 grm., showing no marked alteration. Spleen *nil*. Both kidneys slightly granular, cortex somewhat mottled and slightly hæmorrhagic in appearance. Adrenals disintegrated. Pancreas extraordinarily long from head to tail. The head is swollen and on section shows areas of hæmorrhages in its substance. There are several small whitish areas about the size of a pin's head scattered throughout the fat in the immediate neighbourhood of the gland. Pancreatitis hæmorrhagica acuta (?) Small intestine: Several areas of petechial hæmorrhages beneath the mucous membrane. The uterus shows one small pedunculated fibroma. Left ovary cystic.

(3) *Microscopical Examination: Material and Methods.*

The brain (except the right hemisphere), the spinal cord with the spinal ganglia, a sympathetic ganglion from the lumbar plexus, the hypophysis, different parts of the thyroid, the parathyroid, pancreas and pieces of the heart, liver, spleen, and kidneys, were removed and preserved in a weak formalin solution. The right cerebral hemisphere was kept for chemical determination of the amount of calcium salts. Small pieces from the left frontal cortex, from Broca's area, and from the anterior central convolution (tongue, facial, and leg area), and from the cerebellum, from the medulla oblongata, and the spinal cord at different levels, several spinal ganglia (cervical and dorsal) and the sympathetic ganglion were cut in sections by the paraffin and celloidin methods, and stained with Nissl, Bielschowski, Weigert, and Marchi methods. Sections of the other organs were stained with hæmatoxylin-eosin and Van Gieson's methods; some sections from the pancreas were also examined by Gram's method.

(a) *Organs.*—Thyroid gland (fig. 3): The most striking change to be seen is an extreme atrophy of the glandular substance, and the colloid material was almost absent. The gland consists almost exclusively of dense fibroid tissue, and of foci of round cells scattered here and there like small islands. These crowds of round cells, as a rule, surround and include the small remaining portions of glandular epithelium. There are also in the centre of the islands of small round cells, large round epithelial cells, which are partly isolated, partly huddled together in little groups, but, as a rule, exhibiting no lumen, corresponding to the centre of acini. Very rarely, but here and there, may be found

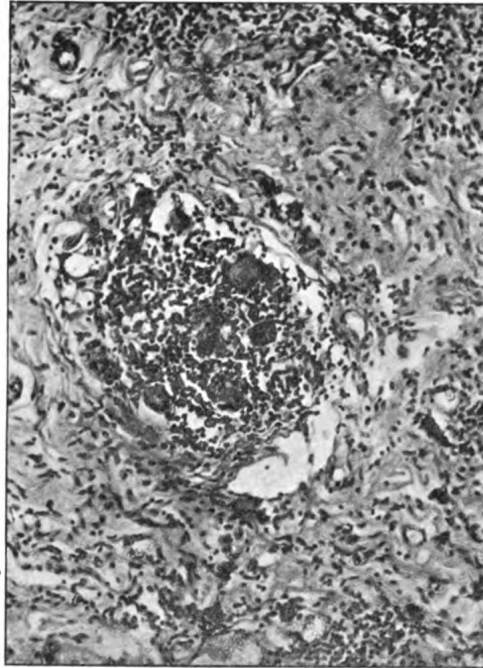


FIG. 3.

Section of thyroid gland from Case III. (Magnification 140.)

an atrophic acinus with a small lumen containing a little colloid. Parathyroid: Epithelial corpuscles are well seen, but there is also a marked increase of lymphoid tissue as described above in the thyroid gland. Some of the epithelial corpuscles seem to have hypertrophied, forming true acini with a comparatively wide lumen filled with a homogeneous colloid-like mass. Hypophysis cerebri (fig. 4). The pituitary body, although perhaps slightly hypertrophied, shows the usual structure of its cerebral and its glandular lobule. The chromophile cells are not markedly increased in number. The intermedial part is very richly vascularized, and seems to contain rather more colloid substance in its cysts than usual, the cysts being surrounded by small cubical and very chromophilous cells. Pancreas: Sections stained by hæmatoxylin-eosin exhibit irregular but fairly sharply limited clear patches to the naked eye, which seem in preference to have their seats in the neighbourhood of the principal fibrous and vascular septa. They correspond to foci of necrosis affecting the glandular tissue, whose cells, in those patches, are very faintly stained with a pale and often indistinct

nucleus. In the septa, and partly also infiltrating the necrosing parenchyma, there are numbers of diffuse hæmorrhages and coagulated masses of hæmorrhagic exudation. A diffuse and not very dense infiltration of round cells can be seen everywhere, but especially in the neighbourhood of the septa. In the fibrous tissue (which seems to be somewhat increased) many areas of a homogeneous appearance can be seen, staining deeply red with Van Gieson (connective tissue fibres in a state of hyaline degeneration). The muscularis of the larger ducts is thickened and partly in a condition of hyaline degeneration. With

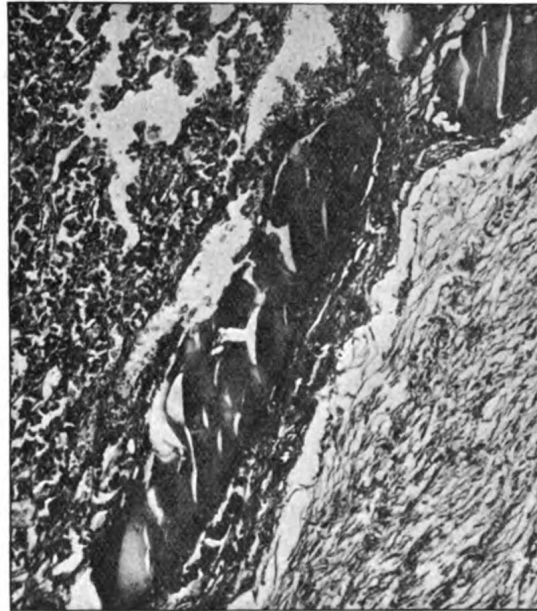


FIG. 4.

Section of the pituitary body of Case III. Between the light cerebral portion of the gland and the dark glandular portion is seen an abundance of colloid material, filling, as it were, a sinus. (Magnification 120.)

Gram's method a few diplococci (Gram-positive) can be seen lying free in the tissue. Beside these there are many saprophytes of all kinds which beyond doubt are of post-mortem origin. The liver shows nothing of importance excepting perhaps a slight increase of connective tissue. The heart and the spleen do not reveal any change. Kidneys: There is an intense hyperæmia, and here and there small capillary hæmorrhages can be seen. In some parts the epithelium appears to be

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swollen up, but the nuclei are well seen. No increase of fibroid tissue.

(b) *Nervous System*.—It may be desirable to mention that the preparations stained with Weigert and Marchi methods did not reveal any degeneration of the myelin sheaths surrounding the nerve-fibres in this case, and the changes described relate, therefore, to the appearances presented by the various groups and systems of ganglion cells.

Preparations of the Central Nervous System stained by Nissl and Bielschowski Methods.

(1) *Cerebral Cortex*.—(a) Anterior central convolution: Nearly all Betz cells of the leg area show a certain amount of chromatolysis, but of a very varying degree of intensity. In the least affected cells the Nissl granules are still well shown, but the staining is more or less diffuse. Most of the cells, however, are in a more advanced stage of the chromatolytic change; the most frequent alteration met with being a central chromatolysis, the nucleus as a rule remaining still in the centre, but decreased in volume, and very often showing nothing more than the nucleolus (fig. 5). When the cell shows a total chromatolysis the nucleus is nearly always eccentric; the dendrites are missing or broken off. None of the cells are swollen up. In the advanced forms of chromatolysis a marked increase of yellow pigment is seen, which often occupies nearly the whole of the cell except the deeply stained periphery. There are only a very few completely disintegrated cells to be seen. The other cell layers of the motor cortex do not show any marked changes except a certain amount of hyperchromatosis (diffuse staining). The Bielschowski preparations show the fibrils generally well preserved. Facial area, and tongue and larynx area: These show about the same degree of chromatolysis of their Betz cells as the leg area.

(b) Frontal cortex: The small pyramidal cells of the frontal convolutions are mostly somewhat diffusely stained, but show neither definite chromatolysis nor any nuclear changes.

(c) Broca's convolution: There is some chromatolysis of the middle-sized pyramidal cells and of the cells of the multiform layer, but both of a slight degree only. (No total achromatosis.) We do not, however, consider these cortical cell changes sufficiently definite to be associated with any clinical symptoms manifested during life.

(2) *Cerebellum*.—The greater number of Purkinje's cells are unaffected; yet, among those apparently healthy cells, here and there a specimen in a more or less advanced stage of chromatolysis can be detected, but without ever showing nuclear eccentricity. By the Bielschowski method no definite changes are to be seen.

(3) *Medulla Oblongata (Medium Third)*.—The most marked changes occur in the medulla, where all the different ganglia, without exception, are affected, but in very varying degree of intensity. In the nucleus of the twelfth nerve the cells are generally only in the first stage of

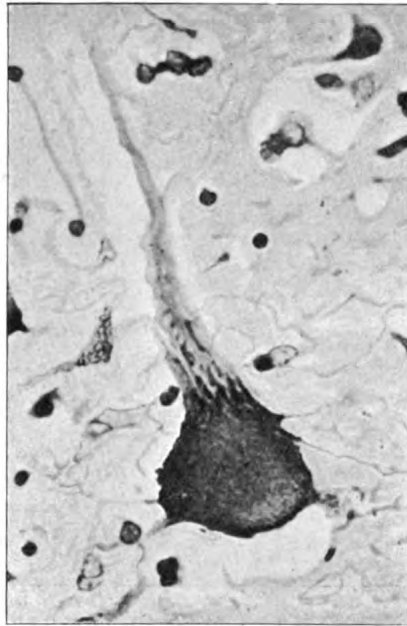


FIG. 5.

Section of motor cortex showing central chromatolysis of a Betz cell; the nucleus is indistinctly seen in the centre. Nissl stain. (Magnification 550.)

chromatolysis, showing no nuclear eccentricity, and no total loss of the Nissl granules. (Plate—3.) Here, too, the vagus system is by far the most severely affected, even more seriously than in the first case; in the dorsal vagus nucleus all the cells are throughout in a terminal stage of chromatolysis (fig. 6), most of them showing a total loss of chromatin and small oblong nuclei peripherally situated, or no nucleus at all. There are also numerous remains of completely disintegrated cells without nucleus or any other definite structure. No normal cells

can be detected. Likewise, in the nucleus of the solitary tract (Plate—2) all the cells are in advanced chromatolysis, and so they are in the nucleus ambiguus (Plate—1, *b*); yet, in the latter, the changes are not quite so grave as in the first, or in the dorsal nucleus of this case. The big “marginal cells” of the descending fifth root nucleus are in advanced chromatolysis. All other structures are less affected. The nuclei of the posterior columns exhibit very various degrees of chromatolysis of their cells, but only a few cells are in the terminal stage. Burdach’s nucleus is more severely affected, except its external

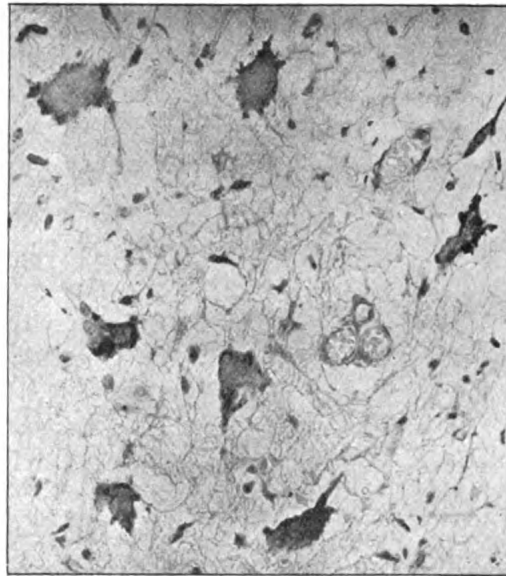


FIG. 6.

Cells of the vagus nucleus showing advanced central chromatolysis. Section of medulla oblongata of Case III; stained by Nissl method. (Magnification 330).

groups belonging to the cerebellum (Monakow’s magno-cellular nucleus and nucleus restiformis, Gudden), in which the alterations are not so grave. The cells of the olivary bodies are mostly in advanced, but hardly ever total, chromatolysis, showing eccentric nuclei and an excess of yellowish pigment. The different association nuclei of the formatio reticularis are, generally speaking, affected in a moderate degree; there are (comparatively to other structures) numerous big multipolar cells with their Nissl granules well preserved.

(4) *Spinal Cord*.—In the cervical cord there is advanced chromato-

lysis of almost all the anterior horn cells without marked preference of any special group being noticeable; yet the middle cells and the fusiform cells of the posterior horns are less affected. In the dorsal cord the motor cells show generally the same degree of change as in the cervical region; the smaller cells of the lateral horns of the dorsal region, which give origin to the fine medullated (sympathetic) fibres, are especially affected. The cells of Clark's columns show throughout marked changes. In the lumbar cord the motor cells are generally rather less affected than in the higher levels of the cord.

(5) *Spinal Ganglia*.—All cells of the spinal ganglia which have been examined are somewhat more diffusely stained than usual. In

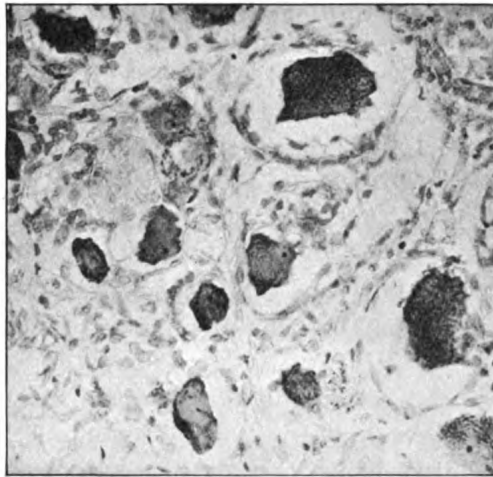


FIG. 7.

Section of dorsal posterior spinal ganglion, stained by Nissl method.
(Magnification 250.)

the cervical ganglia only a very few cells are in a state of more advanced chromatolysis; if so, the capsular cells surrounding them are found slightly proliferating and filling up a part of the pericellular space. The smaller cells, which are supposed to have a relation to the sympathetic, are generally in a stage of hyperchromatosis or definite chromatolysis with eccentric nucleus. Numbers of cells show marked increase of yellow pigment. In the dorsal spinal ganglia a great number of the small cells show advanced chromatolysis with nuclear displacement, and more or less total absence of chromatin (fig. 7); most of them are shrunken, but the capsules do not show proliferation.

The big cells, too, are rather more affected than in the cervical ganglia, yet most of them have their nucleus in a central position.

(6) *Sympathetic Ganglion from the Lumbar Plexus* (Plate—4).—About two-thirds of the cells are in advanced chromatolysis; they are either faintly and diffusely stained with blue or hyperchromatic; a great number are shrunken and without nucleus or show an indistinct nucleus at their periphery. The interstitial connective tissue is very rich in nuclei. There is no proliferation of capsular cells.

(4) *Résumé and Conclusions from Case III.*

A woman, aged 37, of whose previous life not much is known, beyond the fact that she had been in bad health for some years, starts with an acute psychosis, with symptoms of both depression and mania, and corresponding, perhaps, to the clinical picture of a so-called "melancholia agitata." At the Claybury Asylum, where she was admitted, one of us (Dr. Mott) detected certain symptoms of myxœdema which led to a thyroid medication, but without any improvement. Three days before death the pulse suddenly grew extraordinarily slow, never rising above 48. The temperature became subnormal, and a complete inability to swallow food established itself, which was probably the cause of an inhalation broncho-pneumonia, that led to a rapidly fatal termination.

Therefore, here again, as in the two previous cases, we are dealing with a final and grave complication, whose symptoms strongly point to a severe functional disturbance of the autonomic bulbo-motor system, and in particular of the vagal centres. And again, as in the first case, we have found this presumption confirmed by the presence of even more advanced changes affecting the bulbar centres, especially the vagus nucleus, the dorsal vagus nucleus being almost in a state of disintegration.

Beyond these maximal and most striking changes in the vagus system there is a universal chromatolysis throughout the whole nervous system, sparing no structures entirely, but affecting them in very varied degree of intensity; for in the cerebellum, for example, only comparatively few cells are severely attacked, whilst the great majority seem to be quite healthy. Another fact worthy of special mention are the changes found in the spinal and sympathetic ganglia. It is noteworthy that the smaller sympathetic cells were the most affected in the spinal ganglia, possibly indicating, together with the

marked changes in the cells of the sympathetic ganglion, an elective affinity of the morbid process for the sympathetic and vagal systems. We shall refer to this interesting point later on.

The comparatively advanced cell changes found in the nervous system in this case seem to be correlated with the extreme atrophy of the glandular tissue and almost total absence of colloid substance in the thyroid. In respect to the acute hæmorrhagic pancreatitis, we are inclined to regard it merely as a complication secondary to the broncho-pneumonic changes, with commencing gangrene in the lungs. It may be reasonably assumed that it was thus caused by a secondary infection by way of the diaphragmatic lymphatics. In favour of this view there are two facts: firstly, the presence of small Gram-positive diplococci in the pancreatic tissue; and secondly, the adherence of the posterior surface of the left lung to the pleura.

CRITICAL DISCUSSION AND SUMMARY.

Finally, it remains for us to discuss certain points which were found common to all the three cases which have been under consideration, for an analysis of those common points will perhaps enable us to arrive at a more definite conclusion regarding the pathogenetic connexion of the changes found in the nervous system with certain symptoms of the disease, and with the supposed morbid cause in general.

As we pointed out, the clinical aspect common to all three cases was a final and somewhat sudden aggravation of the morbid condition associated with grave and obvious symptoms of a disturbance in the autonomic vagal system of the bulb. Yet there is an interesting difference in respect to the special features of those vagal attacks in the three cases. In Case I, as will be remembered, we were dealing with a complete vago-glosso-pharyngeal paralysis, embracing as well the cardiotonic function, also the functions of swallowing and of articulate speech, whilst in the second case there was merely a certain degree of excitement of the first—the cardiotonic function. In the third case an obvious dissociation between the different vagal functions took place, the swallowing faculty being paralysed, whilst the cardiac apparatus still remained in a state of intense hyper-excitement (bradycardia).

The direct cause of these vagal crises was found in each case, as far as the medulla could be examined, to be an exceptionally grave chromatolysis throughout the cells of the different nuclei belonging to the bulbar, glosso-pharyngeus and vagus systems. Owing to the general

extent of these changes we can, of course, advance nothing in favour of a special localization of the different functions in question in one or other of these nuclei.

This partial bulbar paralysis confined especially to the vago-glossopharyngeus system may be a comparatively frequent complication in terminal myxœdema, owing to the fact that it occurred in two of the three cases here recorded, and an explanation may be asked, therefore, why the autonomic bulbar apparatus is so affected in myxœdema. We may advance two theories in explanation thereof: Either it may be due to a specific chemical affinity of the respective cells to a supposed myxœdematic toxin, or it may be the result of the earlier and more complete wearing out of these automatic centres, due to the fact that no rest is allowed to them, but that they have to go on functioning continually even under the most unfavourable conditions of general metabolism. Against the first supposition of a specific toxic affinity stands the fact that we are hardly entitled to speak of an elective lesion of the vagus system in our cases, since all the other structures, not only bulbar but also cortical and spinal, are likewise, though generally much less, affected. Further, we must emphasize here the point that the toxic nature of myxœdema is far from being an established fact, but, as Biedl¹ in his valuable lectures pointed out, both the clinical aspect and the favourable effect of thyroid medication of the disease clearly seem to indicate that the disease arises from a privation of certain substances necessary to general metabolism. We are therefore inclined to attribute the changes not to intoxication but rather to a chronic starvation of the neurones. Kocher, whose views regarding Graves's disease are well known, recently, in a discussion on the thyroid question,² expressed the opinion that both cretinism and myxœdema were the result of a hypo-function of the gland tissue.

Moreover, Asher and Flack³ were able to show that the thyroid secretion acts directly upon the autonomic and the sympathetic nervous systems, the action upon the latter being more marked. Now in our third case we found, as will be remembered, the sympathetic cells not only in their own, but also in the spinal ganglia and the lateral horns of the spinal cord were severely affected by the chromatolysis, and it might

¹ Biedl, "Innere Sekretion," *Wien. Klinik.*, 1903, xxix, Heft. 10 u. 11, pp. 281-338.

² "83. Versammlung des ärztl. Centralvereins, 1912," *Correspondenzbl. f. Schweizer-Ärzte*, Basel, 1913, xliii, p. 298.

³ Cit. from his volume on the same place.

be suggested that perhaps the deficiency of the normal stimulating action which the thyroid secretion exercises upon both the autonomic vagus and the sympathetic cells may account for the more marked changes presented by the cells in these centres.

A last fact to which we should like to call attention is the comparatively frequent coincidence of the myxœdematous syndrome with an acute psychosis, starting suddenly, as in our two last cases, and mostly having the character of a melancholia or a manic-depressive excitement. Cases, though rare, have been recorded of genuine manic-depressive insanity associated with myxœdema,¹ which seems to indicate that in this form of psychosis changes in the thyroid gland might be found. On the other hand, the connexion between the climacteric involution of the female sexual organs with both melancholia and myxœdema is well known, so that perhaps the primary cause of both affections may be dependent upon a departure from the normal balance of the hormones of the sexual and ductless glands.

FINAL RÉSUMÉ AND CONCLUSIONS.

(1) The changes in the nervous system in myxœdema consist in a general chromatolysis of the nerve cells of a subacute character and secondary to the disease.

(2) These changes, though general, are not of the same intensity throughout the different ganglionic structures, but they seem to affect in a particularly grave manner the autonomous bulbar-motor system (nuclei of the ninth and tenth nerves), and in second line, the cerebro-spinal motor neurons and the sympathetic system.

(3) Clinically, the affection of the vago-glosso-pharyngeal system can lead to severe vagal attacks, or, in advanced cases, to a fatal acute bulbar paralysis.

¹ Tomaschny, "Ueber myxœdematöse Hautveränderung als Parallelvorgang bei manisch-depressiver Psychose," *Neurol. Centralbl.*, Leipz., 1909, xxviii, p. 187.

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[We desire to acknowledge our indebtedness to Major Fink, I.M.S., for the coloured drawings.]

FATAL PELLAGRA IN TWO ENGLISH BOYS, WITH THE
RESULTS OF THE PATHOLOGICAL INVESTIGATION
OF ONE CASE.

BY CHARLES R. BOX, M.D. AND F. W. MOTT, F.R.S.

*(Papers read at a Meeting of the Society of Tropical Medicine and
Hygiene, Friday, February 21st, 1913.)*

On September 20th, 1912, a lad, E.T. of eight was admitted to St. Thomas's Hospital under the care of Dr. Box. The parents feared that he was developing an obscure nervous disease similar to one which had affected his brother for several years, and finally carried him off at the age of thirteen in the year 1911.

The present patient was born at Leyton, in Essex; later resided for five years at Catford, in the suburbs of London, and finally removed with his family to Slough. His father and mother are English and not related to each other. His father is an army pensioner, and for the last eighteen months has suffered from aortic disease. The mother is quite healthy.

Besides the patient they have had nine children. Five of these are living. One died of laryngeal diphtheria; one of an acute toxæmia, after an illness of 24 hours; and one, to whom reference will be made later, from an illness which was no doubt pellagra.

The patient's nervous symptoms were first noticed in June, 1912, three months before he came under observation, when he "fainted" whilst playing cricket. The "faints" recurred on several occasions. Later on twitching movements of the limbs were noticed and also a transitory convergent squint.

On Bank Holiday, August 5th, there occurred a new sort of seizure. He had been stooping and suddenly stood erect, threw his head backwards and would have fallen if not caught. The body became rigid but consciousness was not lost. Similar attacks recurred several times, always with a premonitory feeling of giddiness. He had never bitten his tongue nor been observed to foam at the mouth.

Recently he had become more and more unsteady in his movements.

On examination the boy appeared to be of average intelligence. His

memory was good and he answered questions readily, but proved to be of an emotional disposition and easily moved to tears. His weight was 43 lbs., or 9 lbs. below the average for his age. His father attributed this to the failure of his appetite, saying that there was always plenty of food for the family.

He was able to walk, but his gait shewed a mixture of spasm and ataxy. He moved stiffly with his legs wide apart. The feet were raised high from the ground, steppage fashion, and there was a decided tendency to stagger, this being increased by closure of the eyes. Later adductor spasm also declared itself.

On the day of admission, whilst his gait was being investigated, he had one of the seizures which had been described by his parents. His head was stiffly retracted, he became rigid and would have fallen backwards if not prevented. The attack lasted for a few moments only and consciousness was not lost. He cried quietly all the time.

A coarse nystagmus which accompanied all movements of the eyes was always present, and his speech was rather indistinct. These were the only abnormalities of the cranial motor mechanism. The pupils were active and equal. The optic papillæ were quite healthy. Hearing, vision, taste and smell proved to be normal.

Even when lying in bed the muscles of the arms and legs, particularly the latter, were in a condition of moderate rigidity, but they were not wasted, and there was no appreciable weakness. All movements appeared stiff.

It was also evident, particularly when he was being photographed, that irregular, spasmodic movements of small range were apt to appear both in face and limbs, producing slight jerks which suggested the effect of a faradic shock. There were no deformities of the feet or hands, and the spinal column was straight.

All the deep reflexes, both in arms and legs, were increased but no clonus could be elicited. The plantar reflex was always flexor in type. The cremasteric, abdominal, epigastric and corneal reflexes were present.

Sensibility to all forms of stimuli was unimpaired. Subsequently Dr. SANDWITH pointed out that there appeared to be some para-vertebral tenderness which could be elicited by making firm pressure alongside the vertebral spines, on the right side from the second to the

ninth dorsal, and on the left from the seventh cervical to the fourth dorsal.

The boy swallowed both solids and liquids with ease, but all the time he was under observation there was incontinence of both urine and fæces.

With regard to the alimentary system there was an insignificant rawness of the edges of the tongue and an inflammatory condition of the skin immediately surrounding the anus. The appetite was very capricious and the bowels were inclined to be loose, being opened two or three times a day; later there was a more decided tendency to diarrhœa. The cardio-vascular and respiratory systems shewed no signs of disease. The urine contained neither albumen nor sugar.

The patient presented, in addition to his nervous symptoms, a symmetrical erythematous dermatitis of striking distribution which afforded the clue to the diagnosis of his disease. The skin inflammation involved the backs of the hands and wrists, the orbital regions and bridge of the nose, the nape of the neck and backs of the ears, and, to a slight degree, the points of the elbows.

On the face the dermatitis crossed the bridge of the nose, encircled both eyes and spread slightly on to the malar regions. The skin over this area was reddish in colour, resembling acute sunburn. It was somewhat thickened and shewed a decided tendency to desquamate in small branny scales. The eyelids were slightly swollen and conjunctivæ were injected, presenting a lachrymose appearance. The skin of the nape of the neck was less red and rather more scaly, the lateral extensions of the dermatitis behind the ears and to the adjacent mastoid regions were quite symmetrical. The hair of the back of the scalp was dry, lustreless and thin.

The eruption on the hands had a rougher appearance. When viewed from the dorsal aspects it terminated by a sharp margin across the arm, four finger breadths above the wrist. It covered the backs of both hands, extended on to the fingers in less marked form, and on the dorsum of each terminal phalanx assumed a brownish tint which was in marked contrast with the red colour of the rest of the affected area. The nails were healthy but shallow ulcerations were found in several of the interdigital clefts.

The palms of the hands escaped, but the dermatitis shewed a ten-

dency to extend from the dorsum of the wrists across the palmar aspects, especially from the radial side.

At the points of the elbows a brown scaliness of the skin was evident, and, although there was no red eruption on the feet or legs, the skin of the front of each leg when lightly rubbed assumed a very powdery appearance.

When he was first admitted the affected skin had a fairly bright red appearance, but the colour gradually faded to a brownish tint. At no time did he appear to experience either pain or irritation in the affected parts.

The eruption was recognised as pellagra, owing to its resemblance to the photographs in Drs. LAVINDER and BABCOCK's translation of Dr. MARIE's book on the disease. A copy of this work had been presented to Dr. Box by Dr. J. J. WATSON, of Columbia, who visited England in 1910.

As the result of lumbar puncture, 15 c.c. of clear cerebrospinal fluid were withdrawn. The pressure was not increased. The fluid was examined in the clinical laboratory of the hospital, under the direction of Dr. L. S. DUDGEON. No cells were seen, no globulin was found, and the Wassermann reaction was negative.

At the same time the blood was also examined. This also gave a negative Wassermann reaction, and the count was as follows:—Erythrocytes, 3,475,000 per c.m.; hæmoglobin, 65 per cent.; colour index, 0·9; leucocytes, 5,140 per c.m.

Differential count:—Polynuclears, 59·5 per cent.; polynuclear eosins, 1·75 per cent.; small lymphocytes, 28·5 per cent.; large lymphocytes, 5 per cent.; large hyaline cells, 5·25 per cent.

Whilst under observation in the hospital on some days the patient was decidedly more tremulous than on others. Shock-like twitches of the muscles of the face, arms and legs continued to appear. There were no more cerebral seizures, but a tendency to adductor spasm was superadded to the first observed extensor rigidity of the legs. Spasm of the calf muscles also caused a tendency to walk on the toes. The knee jerks remained exaggerated, but no extensor response was ever obtained from the soles, and no true clonus appeared.

The patient vomited on one or two occasions and the appetite was variable, but, notwithstanding this, he put on weight during the first

week, only to lose it again later as he became progressively weaker.

The state of the bowels, tending to increasing looseness, has already been mentioned.

During the latter part of his life he developed slight delusions, believing, among other things, that his father was under his bed.

Until the last three days of life his temperature was practically normal, only rising slightly on one or two occasions.

About a fortnight before death an acute suppurative balanitis made its appearance, but it ultimately became necessary to slit up the prepuce. This was effected under nitrous oxide anæsthesia three days before he died. The patient was very stuporous afterwards, but did to a certain extent regain consciousness. Whilst in this condition the knee jerks remained exaggerated, and a pseudoclonus was obtained at the ankle, but no extensor response from the soles. The jerky movements of the limbs continued to occur at intervals. The pulse now became accelerated and began to fail, whilst respiration was very irregular.

The day after the anæsthetic the temperature rose to 101·6, but soon fell to normal. The next day it barely touched 99·5. On the third day it ran up to 100·4, and the pulse rose to 160. After a short stage of irritability the patient died. The duration of illness was four months.

A post-mortem examination was carried out two and a half hours after death.

The body was not greatly emaciated. Fat was still present in the subcutaneous tissues and in the omenta.

The eruption could still be recognised on the hands and wrists, the elbows, the neck and the face, as a brownish scaly thickening.

The mouth, fauces and tongue shewed no macroscopic lesions. The lower third of the interior of the gullet was bile-stained, but the mucous membrane appeared normal. The gastric mucosa was coated with adherent mucus, but not injected, ulcerated or wasted.

The only striking point in connection with the small intestine was the quantity of mucus present in it.

The edges of the ileo-cæcal valve were purple in colour and superficially ulcerated; the ulceration extended on to the adjacent wall of the cæcum. In the colon itself, near the splenic flexure, was a circular cicatrix, about half an inch broad, and slightly ulcerated at its margin.

The appendix was normal in its proximal two-thirds. A tight

stricture had caused the distal third to become bulbous. It contained inspissated pus.

The mesenteric glands were enlarged; one or two of them contained caseous material which was calcifying. The largest glands were not much bigger than peas.

There was no peritonitis, either old or recent.

The liver was fatty-nutmeg in appearance and not enlarged. The gall-bladder contained dark bile. The weight of the liver was 24 ounces.

The spleen weighed $2\frac{1}{4}$ ounces. It was normal in colour, and the cut surface presented nothing remarkable.

The adrenals and pancreas appeared quite healthy.

The kidneys weighed $6\frac{1}{2}$ ounces. They were a little swollen, and on section had a pale œdematous appearance. Their capsules could be stripped readily.

The bladder, ureters and rectum were healthy. The prepuce had been slit dorsally, and was somewhat thickened from recent inflammation.

The pleuræ and pericardium were free from inflammation or adhesions.

The right and left lungs weighed 4 and 5 ounces respectively. They were slightly over-inflated and everywhere crepitant. No tubercles were found in lungs or bronchial glands.

The heart weighed $2\frac{3}{4}$ ounces. It was free from valve lesions and its muscle dark and firm.

The marrow in the femur and ribs was bright red.

The dura mater was healthy, as also were the great venous sinuses of the brain.

The pia-arachnoid was not œdematous and shewed no signs of opacities. The spinal meninges also were healthy.

The ventricles of the brain were not distended, and it was difficult to be sure of any sclerosis of the cord before hardening.

A culture made from the blood immediately after death shewed, according to Dr. DUDGEON'S report, the presence of streptococcus pyogenes.

History of the brother's fatal illness.—R.T., age eleven years, was admitted to St. Thomas's Hospital under the care of Dr. Box, on September 27th, 1910, and remained under observation for a fortnight

only. He was the sixth child of the family and, unlike his brother, was born in Kilkenny, but only resided there for five months, the family leaving that part thirteen years ago and removing to Essex.

For several years, possibly six, he had been getting weak on his legs, and was dull and backward with his studies. He suffered with incontinence of urine. Latterly he had become worse in every way and for a few weeks his speech had been indistinct.

In hospital he mostly lay curled up in his bed. His mental condition was dull. He was very slow to answer questions and easily moved to laughter. His voice was low-pitched, and he said he could not speak loudly.

There was marked weakness of both arms and legs, but no picked-out atrophy of muscles. There was also a tendency to spasticity, particularly in the lower limbs.

When he attempted voluntary movements with the hands a coarse intention tremor was noticeable. When he tried to walk his movements were very unsteady; he shewed a marked tendency to sway laterally and almost over-balanced when he turned round.

Movements of the eyes were not limited in any direction, but lateral movements were accompanied by a coarse nystagmus. The optic papillae, fundi and media were quite normal, but a high degree of hypermetropia was present in both eyes. The pupil reactions were sluggish but complete.

All the arm reflexes were decidedly brisk. The knee-jerks were exaggerated, especially on the right side. No clonus was obtained in the lower limbs, but the plantar reflexes were both extensor in type and there was a double claw-foot.

Deglutition was normal. With regard to micturition, sometimes the urine was retained, sometimes there was incontinence.

No defect in cutaneous sensibility could be discovered.

The chest was well-formed and its movements good. No pulmonary disease was found.

The heart's area was not increased. There were no murmurs. The pulse was regular and varied from 72 to 96.

The temperature was normal throughout.

The only anomaly in the digestive system lay in the action of the bowels. At first these were constipated and enemata necessary. Later

there was a somewhat troublesome diarrhoea which needed treatment.

The blood was examined for a Wassermann reaction with negative result, and the cerebro-spinal fluid showed no globulin and no Wassermann reaction. Not enough for a cell count was obtained.

But little is known about the eruption. It was not specifically described in the notes, or indeed specially noticed in hospital, but in the state on admission he is described as being of a high colour and somewhat tuberculous facies, whilst later a compound tar ointment was prescribed, presumably for the face. We have since learned from his mother that he did have a rash which appeared three or four years before he came under observation at the hospital; that this rash appeared in the summer only on successive years; but that it was not so pronounced as the rash in his brother's case. It involved the face, neck and the hands, but did not cause any septic spots between the fingers.

The boy was discharged in fourteen days in much the same condition as when admitted, the disease being diagnosed as an anomalous form of combined degeneration of the cord in some respects resembling Friedreich's Ataxy. No suspicion of pellagra arose at the time.

We heard later that he died in January, 1911, but could not ascertain from the parents the immediate cause of his decease. The duration of illness was over six years. No post-mortem examination was made.

Both boys were said to be fond of "pop-corn," or parched maize, but only had means to buy it occasionally.

THE HISTOLOGICAL CHANGES IN THE NERVOUS SYSTEM
OF DR. BOX'S CASE OF PELLAGRA COMPARED WITH
CHANGES FOUND IN A CASE OF PELLAGRA DYING IN
THE ABASSIEH ASYLUM, CAIRO.

By F. W. MOTT, F.R.S.

METHOD EMPLOYED FOR PREPARATION OF SPECIMENS.

The brain, spinal cord, and a few of the posterior spinal ganglia and a small piece of the sciatic nerve were sent for examination. Portions of tissue obtained from various parts of the central nervous system were separately hardened and fixed in Muller's fluid for subsequent examination by the Marchi method for recent degeneration, and by the Weigert and Weigert Pal methods for fibre system degenerations. Other portions were hardened for a few days in 5 per cent. formalin, and transferred to alcohol in successive strengths for examination by Nissl method; some portions of the formol fixed tissues were subjected to the Bielschowsky method for demonstration of fibril changes in the cells.

The Muller hardened tissues were treated by the celloidon method before sections were cut by the Jung microtome.

The formol hardened specimens were embedded in paraffin and cut in the Cambridge rocking microtome. The sections were 10μ in thickness.

CHANGES OBSERVED IN THE FIBRES BY THE MARCHI METHOD.

Sciatic Nerve.—Recent scattered degenerated fibres were found in all the longitudinal and transverse sections of the sciatic nerve; not limited to any bundle of fibres, but general, though somewhat unequal in numbers in all. *Fig. 1* shews one of these bundles in transverse section; the black dots are the degenerated fibres. *Fig. 2*, a bundle in longitudinal section. Owing to the piece of nerve not having been pinned out on cork when placed in the hardening fluid before I received it the fibres are curled, consequently the sections have cut many of the fibres obliquely.

Cauda Equina.—The roots of the *cauda equina* shew similarly scattered degenerated fibres (*vide Fig. 3*).

Spinal Cord.—There is general diffuse and scattered degenerated

fibres throughout the white matter, more marked in the postero-lateral and posterior median columns than elsewhere.

CHANGES OBSERVED IN THE FIBRE SYSTEMS BY THE WEIGERT AND
WEIGERT PAL METHODS.

There is a slight general diffuse sclerosis throughout the white matter of the cord in all regions, but in certain regions there is a perceptible naked eye combined sclerosis affecting the direct cerebellar and Gower's tracts, Goll's column and the crossed pyramidal tracts. The ascending degenerations are very observable, as *Figs. 4 and 5* shew in the cervical region. This is to be expected, because in this region all the fibres belonging to these tracts have taken up a definite position, consequently disappearance of the fibre and replacement by neuroglia tissue is more obvious to the naked eye, but microscopic examination in any part of the cord shews the outfall of fibres in these systems and their replacement by neuroglia.

The descending degeneration in the crossed pyramidal tracts is obvious to the naked eye, but, aided by a hand lens, is very evident in the lower lumbar and sacral regions (*Fig. 6*). *Figs. 7 and 8*—Examination microscopically shews an outfall of fibre and replacement by glia tissue of the crossed pyramidal systems in any part of the course. The direct tract is much larger on one side than the other, and in the cervical region a well-marked outfall of fibres with sclerosis is observable with a low magnification. This is more obvious on the side where the direct tract is the larger. Some scattered sclerosis can be observed in the pyramids of the medulla.

CHANGES OBSERVED IN SECTIONS OF THE CEREBRUM, CEREBELLUM,
PONS, MEDULLA, SPINAL CORD AND SPINAL GANGLIA CUT BY THE
PARAFFIN METHOD, AND STAINED BY NISSL, POLYCHROME, GIEMSA,
LOGWOOD, EOSIN AND VAN GIESON METHODS.

It may at once be said that in none of the sections examined was there any evidence of meningeal or perivascular infiltration with lymphocytes or plasma cells or with polynuclear leucocytes. I mention this, firstly, because the terminal streptococcal infection had, therefore, not invaded the cerebro-spinal fluid, and could, therefore, as there was no inflammatory sign, account for the changes in the neurones. Moreover,

the absence of chronic meningo-encephalitis and myelitis, so characteristic of protozoal diseases, *e.g.*, malaria, in which the vessels may be filled with the organisms and yet no inflammatory perivascular and meningeal reaction is seen, so that it in no way disproves a protozoal origin of this disease; moreover, although all the changes are like those produced by a chronic toxæmia, yet the cause of that toxæmia has not been satisfactorily determined. Whether the two ulcers found in the intestines had any relation to a chronic toxic infection it is difficult to say. The combined sclerosis is not unlike that found in a pernicious anæmia which we know may be due to a streptococcal toxæmia.

By any one of the methods mentioned the following changes may be observed :—

All the posterior spinal ganglion cells shew in varying degrees a marked chromatolysis, swelling of the cell, disappearance of the Nissl granules, except at the periphery, and frequently eccentric position of the nucleus (*Fig. 9*). All the anterior horn cells and their homologues in the medulla and pons shew varying degrees of perinuclear chromatolysis; in some instances the cells are so markedly swollen, and the nucleus is so eccentric, that it appears as if the cell were dead. There was a marked chromatolysis of the cells of Clarke's column.

The Betz cells of the cortex shewed similar changes but not so marked (*Fig. 10*); likewise the cells of Purkinje; the pyramidal cells of the cerebral cortex did not appear to be markedly affected.

Wherever the nervous system was examined the cells which normally have a Nissl pattern seemed to shew a change in the nature of a disappearance of the granules partial or complete, without any evident changes in the vessels of an inflammatory nature to account for the same. Seeing that there is a combined sclerosis of the cord, obviously these changes could not be of quite recent origin, and, therefore, capable of being explained by the terminal generalisation in the blood of streptococci from the balanitis. Moreover, my experience tells me that the nerve-cell changes rather indicate a chronic toxæmia.

CHANGES OBSERVED IN THE CELLS BY BIELSCHOWSKY

FIBRIL METHOD.

The anterior horn cells and the cells of Purkinje, also the Betz cells, but to a less degree, shew in varying degrees, in different parts of

a section and in various regions examined, fibril changes similar in character. Some cells shew hardly any fibrils, others a few, others appear quite normal, as if they had been attacked in different degrees of intensity by the poison. This is not an unusual condition of things in chronic toxic conditions affecting the nervous system. *Fig. 11* shews the changes in the cells of Purkinje. *Fig. 12* shews a group of anterior horn cells.

Comparison of these changes in the cells of Dr. Box's case with those of a pellagrous patient who died at the Abassieh Asylum—for the notes and material of which I am indebted to Dr. PEARSON—shew that there is no essential difference. There is a combined sclerosis of the spinal cord more marked in the Egyptian case; there are the same changes in all the ganglion cells of the spinal cord and brain, and there are no signs of acute or chronic vascular or meningeal inflammatory changes. This case came from a district where the maize which the people had eaten was very bad. My assistant, Mr. MANN, has made a preliminary examination of this maize, and he finds that compared with sound maize there was a considerable diminution of phosphorised lipoids. It is possible that any impoverishment of diet, by which certain essential substances in the blood fall below the physiological minimum, may play a part in a degenerative process of the nervous system. Still, here we find these two cases of Dr. Box, in which diseased maize certainly could not have played any part in the production of degeneration of the nervous system, similar in histological details to those of a case which had come from a pellagrous district in Egypt, where unsound maize had been a staple article of diet. It seems that we must look for some other etiological factor as the essential cause of this disease, and we can but admire Dr. SAMBON's enthusiasm and energy in the endeavour to shew the protozoal origin of this disease by its epidemiology.

I wish to express my indebtedness to my assistant, Mr. CHARLES GEARY, for the photomicrographs and preparations.

REPORT OF EGYPTIAN CASE.*

By DR. R. W. J. PEARSON.

Setabbhoocha Abdalla, native woman, belonged to the Mudirieh of Menoufieh. Nationality, Egyptian; age, 30 years; religion, Moslem. Not addicted to alcohol or hasheesh. First attack: admitted 18th September, 1911: died 16th November, 1911. Bodily state on admission: height, 150 cm.; weight, 6 stone; nutrition, bad; temperature, 37.1° C.; facial expression, sad; eyes—pupils round, central and equal; both eyes react to light and accommodation; pulse—weak, small and quick, 120 per minute; heart—pulmonary sound accentuated, otherwise normal; tongue—clean and steady; lungs—slight rhonchi in right lung near apex; respirations—17 per minute; bowels—has diarrhoea. Extremities—pellagrous rash over dorsum of hands and back of forearms, over dorsum of feet, over the knees, and the backs of the elbows. Nervous system—reflexes; knee-jerks exaggerated; no ankle clonus nor Babinski; speech—she speaks in syllables, due to weakness; gait—affected, due to weakness; sleep—good. Mental—does not know the day nor date, she speaks fairly sensibly; says she came to Cairo for her illness; does not see visions nor hear voices.

19th September, 1911. The patient has a dull melancholic expression. She is very depressed. She is disconnected in time and space; does not know where she is, or what day or date it is. Her mental reaction is very slow, and she seems to have great difficulty in expressing herself. She is very confused and incoherent. Her physique is below the average and she is much emaciated. She has a pellagrous rash on the face, round the eyes, and across the nose, also on the hands and forearms, feet and legs, knees and elbows. She has a marked tenderness on pressure over the posterior nerve roots. Her tongue is denuded of epithelium, and her parotids are markedly thickened. Her lungs are sound. Her heart has a very feeble action and there are hæmic murmurs at the base. Her chest wall is sound. Her eyes react to light and on accommodation. Her knee-jerks are increased; no ankle clonus nor Babinski's sign. She denies hasheesh and alcohol, and there is no history of them. She says she is very poor and has eaten a lot of dhurra. There are no signs of syphilis. She has pellagrous diarrhoea, and is in a very weak condition. She is not suicidal.

* These Notes were not presented to the meeting.

11th October, 1911. The general condition of the patient has slightly improved. Mentally she is not so confused now, and her mental reaction is quicker than on admission. The pellagrous (black) rash over her nose and eyelids is beginning to peel off, also the rash on her hands and feet. She has a peculiar gait, very like the gait of paralysis agitans, without the tremors of that disease. Her head and shoulders stoop forward in a "hunchback" fashion. Her knees are flexed and she walks flat-footed. Her muscular system is wasted and weak, and the patient supports herself with the skeletal system and ligaments rather than the muscles. The diarrhoea is getting somewhat better. Her tongue is denuded of epithelium. The enlargement of the parotids persists. Her knee-jerks are still, and no ankle clonus nor Babinski's sign. She still has marked tenderness over the posterior nerve roots. Her eyes react to light and accommodation.

26th October, 1911. The pellagrous rash is reappearing in the elbows, but is completely peeled off from the face and hands, leaving a whitish inelastic skin. The patient is getting more shaky and unable to sit up. She has stomatitis; she says she is well and strong.

2nd November, 1911. The patient is helpless and depressed. She is chattering and incoherent; she is in a condition of typhoid pellagra.

16th November, 1911. The patient died this morning at 6 o'clock after prolonged exhaustion.

Extract from post-mortem Notes:—The post-mortem was done on the 16th November, 1911. Condition of body and external appearances—very emaciated, with black pellagrous rash on feet and hands, elbows, etc.: parotids markedly enlarged, and tongue denuded of epithelium; markedly anæmic. Calvarium—450 grms., thickened and dense. The brain was kept for examination later and was not cut at the post-mortem. The dura mater was a good deal thickened and was adherent to the calvarium so much so, that the brain had to be removed with the calvarium still in situ, and afterwards carefully separated from it. There was a distinct excess of cerebro-spinal fluid. The spinal cord below the medulla (where it is cut in removing the brain) had a lot of blackish-brown pigment in the membranes, which was granular to the feel. Heart—160 grms., pale, anæmic, flabby and somewhat atrophied; no organic lesions of the valves; no atheroma of the aorta or coronary arteries. Right lung—

300 grms. ; some pearly old adhesions all along anterior border. At the base of the right lung a small cavity, necrotic in origin, was found ; no signs of tubercle ; congested at base. Left lung—some pearly old adhesions along anterior border and surface of lung ; no signs of tubercle ; congested at base. Liver—1,040 grms ; anæmic, otherwise normal ; gall bladder contained some blackish liquid bile ; no gall stones. One bilharzia worm was found in the specimen of portal blood taken. Right kidney—100 grms. ; somewhat hard and fibrous ; capsule strips easily ; pelvis congested. Left kidney—120 grms. ; capsule strips easily ; somewhat fibrous ; pelvis congested. Spleen—170 grms. ; very congested ; soft and friable. Intestines—the small intestine in normal condition ; the large intestine in condition of chronic colitis with denudation of epithelium and patches of marked congestion with ecchymises and arteriole dilatation of blood vessels. The stomach dilated and thinned with denudation of epithelium. The intestines as a whole shewed the thinning and transparency typical of pellagra.

Special Notes.—The bladder had granular sandy patches of bilharziasis. The spinal cord was removed and preserved for examination. Cause of death—pellagra.

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**The Complete Histo-pathological Examination of the Nervous
System of an Unusual Case of Obstetrical Paralysis
Forty-one Years after Birth, and a Review of the
Pathology.**

By GEO. F. BOYER, M.B. (Toronto).

IN the following paper it is my intention to review the pathology and to describe the results of a complete histological examination of the nervous system of a case of obstetrical paralysis. The work has been done in the Pathological Laboratory of the London County Asylums; and for permission to work in the Laboratory and enjoy the exceptional facilities it offers for research, I am greatly indebted to the Asylums Committee. To Dr. Mott, the Director of the Laboratory, I would also express my thanks for placing this case at my disposal, and for his guidance and encouragement throughout the work.

CASE NOTES.

A. B., female, aged 41, was admitted five and a half years ago to Claybury Asylum suffering from puerperal melancholia, with filthy delusions, accompanied by marked excitement at times.

I have personally interviewed the mother of the patient and obtained the following information: She was a full-term child; the labour was difficult and prolonged. The right arm presented, and for two hours was left with the hand protruding from the vulva; then the accoucheur brought down a leg (? which), and after great traction the child was

delivered. The child was very blue and was resuscitated only after prolonged efforts. The child did not breathe properly for some hours. Very soon after birth the mother noticed the infant did not move the right arm, and this paralytic condition has persisted. As a child sensation in the limb was believed to have been perfectly normal by the mother. The right leg was never weak or paretic during childhood. She was always very healthy and had no acute illnesses. There is no history whatever of anterior poliomyelitis.

The patient was married seventeen years ago and has had four children, two of whom are alive and healthy, and two are dead. There were no miscarriages. Fourteen years ago she became insane after the birth of a baby, but recovered at home in a few months' time after the death of the child. She became insane five and a half years ago on being confined, and was sent to Claybury Asylum where she has remained since. She was well, and of a cheerful and normal temperament during the interval.

Clinical examination on admission to the asylum: The patient was a female of slightly under average stature but with fair nutrition. No cardiac, pulmonary, or abdominal lesions were found. She could walk perfectly well. There was no facial or cranial nerve involvement. There were no external signs of syphilis. The pupils were equal, regular, and reacted to light. The right arm was extremely atrophied and flaccid and was maintained in a position of slight flexion at the elbow. The forearm was in a position midway between pronation and supination (dorsum of the hand looking outwards) and the third, fourth and fifth fingers were flexed on the palm to a relatively increasing extent. The forefinger and thumb were also in a position of moderate flexion. The right shoulder-girdle was atrophied and especially the pectoral muscles. Her right trapezius was quite powerful. She had very little, if any, power in the right biceps. She had some adduction of her arm (could carry a book between her arm and body). There was very slight power of flexion of the third, fourth and fifth fingers. There were never any subjective symptoms about heat or cold and pain in the arm (the afferent impulses were not tested because of her mental condition). She had fair use of her left arm, forearm and hand (could lace her boots and even sew).

During the past three or four years she has been losing power in her right leg; she was much weaker upon it at some times than at others. She could always walk, even up to the time of her death. The knee-jerks were not obtained on either side. A gradual atrophy

of the leg has developed during the past three or four years. She died in November, 1910, of broncho-pneumonia, at the age of 41, after a comparatively short illness and without any marked rise of temperature being recorded.

AUTOPSY REPORT.

The subject was a female of poor musculature and rather small stature. Her weight was 42 kilos (96½ lb.) The autopsy was performed ten hours after death. The body showed no marks of syphilis. The pupils were equal and regular. The right arm was very atrophied. The fingers were all shortened, and the third, fourth and fifth fingers were flexed on the palm. The right leg showed a general muscular atrophy. Mensuration (in inches):—

					Right		Left
Shoulder to thumb	15½	...	19½
Circumference at middle of arm	6½	...	7½
Circumference at middle of forearm	5½	...	6¾
Length of lower limb	33½	...	33½
Circumference at top of thigh	15½	...	17½
Circumference just above knee	11¾	...	12½
Circumference at middle of calf	11	...	12

The heart and large vessels and abdominal contents were all natural. The uterus and tubes showed no evidence of disease. The lungs showed a well-marked bilateral broncho-pneumonia without any signs of tuberculosis. The calvaria was normal. The meninges were natural, except the arachnoid mater, which was slightly less transparent than normal. No macroscopic brain lesions could be found; the cerebral vessels showed no changes. The cortex was of average pattern. No differences of size and shape could be found between the motor areas of the two hemispheres.

Brain (weight as a whole)	1,295	gram.
Right hemisphere	560	„
Left hemisphere	565	„
Cerebellum, pons and medulla	150	„

The upper end of the central fissure on either hemisphere ran into the mesial, and both sulci were of about normal depth and length. The superior genua were easily found on both sides. The inferior genua were fairly well marked. The great annectant gyrus was present on either side. There was no constant difference in the thickness of the

cerebral cortex, between the corresponding areas of the leg, arm and face of either side (all areas varying from 2.5 mm. to 3 mm. in thickness). The crura cerebri and the cerebellar hemispheres were of equal size on both sides.

The spinal column was normal. The whole spinal cord appeared natural except the right side of the cervical region where the meninges were thickened, very dense and tough and adherent to the cord substance over the region of the fifth, sixth, seventh and eighth cervical and the first dorsal segments. These thickened meninges extended slightly to the left of the median line on the anterior aspect of the cord. The thickening and adherence was most marked in the region of the seventh cervical roots and gradually decreased above and more rapidly disappeared below that level. In this process the anterior roots have suffered most and they were reduced in length to a varying extent and were entirely obliterated at the level of the seventh cervical root on the right side. The posterior roots were shortened and small. The right anterior horn zone was flattened and specially so at the level of the seventh cervical, thus making the right half of the cord much smaller in size. The anterior and posterior root bundles of the left side appeared natural.

The posterior cervical ganglia of the fourth, fifth and seventh cervical and the second dorsal roots showed no change on either side from the normal, except that the seventh cervical on the right side was reduced in size.

The brachial plexus of the left side appeared normal in size and in origin. The roots of the fifth, sixth, seventh and eighth cervical on the right side were much smaller than natural, and were reduced to fibrous cords which were impossible of good dissection, owing to the abundance of tough fibrous tissue suspending some fat in its integument. The eighth cervical root was larger than the fifth, sixth or seventh, while no difference could be noted between these latter three. The right plexus was much smaller than the left. There was no difference in size between the median and the ulnar nerves from the forearm of either side. Unfortunately the muscle tissue removed for examination of the muscle spindles and the cervical sympathetic ganglia were lost.

Technique.—The brain after removal was placed into 5 per cent. formalin for forty-eight hours, then the motor cortex on either side was divided into three areas according to the plan adopted by Campbell [5] in his investigations of the cortex in amyotrophic lateral sclerosis. The leg (or upper motor) area consisting of the precentral gyrus on the

mesial surface, with the external convex surface down to the level of the superior genu; that for the arm (or middle motor) area being that part of the precentral convolution between the superior and the inferior genua. The whole of the middle motor area of the left side was sectioned, also nearly all the superior motor area. Specimens were removed at different levels of all areas and serial sections examined. The cortex was stained by the Nissl, polychrome blue and Van Gieson methods for cells; by the Ranke, Heidenhain and Cajal methods for neuroglia; by Scharlach R and Sudan III for fat; by Bielchowsky's

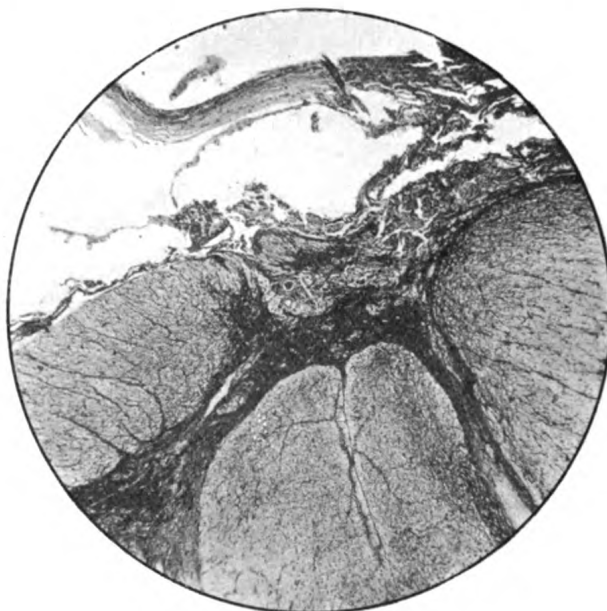


FIG. 1.

Photomicrograph showing fibrosis in the anterior median fissure and destruction of the right anterior horn of grey matter at the level of the seventh cervical segment. (Ranke, Victorian blue stain.)

method for neurofibrils; and by the Weigert-Pal method for the cortical fibre systems. The spinal cord was kept in 5 per cent. formalin solution for a week and then all levels from the second cervical to the third sacral segments were examined by the Nissl and Weigert-Pal methods; and sections at various levels were stained by the Ranke, Cajal and Bielchowsky methods and by Scharlach R. The fourth, fifth, seventh cervical and the second dorsal posterior root ganglia were stained by Weigert-Pal and then the Nissl or Van Gieson method used

as a counter-stain. The brachial plexuses were cut transversely at the point where the posterior roots of the upper, middle and lower cords unite to form the musculo-spiral nerve, and, with the median and ulnar nerves of each side, were stained by the Weigert-Pal method.

Histological changes at the site of the lesion.—Microscopic sections show that the thickness of the meninges (to which reference has already been made) is due to the formation of firm and densely organized fibrous tissue, which is firmly adherent to the cord at the levels of the lesion, but specially so at the level of the seventh cervical segment. This superficial fibrosis extends even on to the anterior part of the left half of the cord at the level of the sixth, seventh, and eighth cervical roots. The local lesion first becomes noticeable at the level of the fifth cervical segment and is last seen on the surface of the cord at the level of the first dorsal. The maximum cord injury exists at the level of the seventh cervical root on the right side and in the anterior horn area a von Gudden's nerve evulsion was practically produced at the time of the trauma. Nearly all the structures lying in front of the anterior horn of grey matter have been involved in this sclerotic patch, and what still remains of the anterior horn of grey matter lies upon the antero-lateral surface of the cord. In this change not only has the right side been affected; but the grey matter on the left side is seen to be distorted and shrunk, especially at the level of the seventh cervical segment (figs. 1 and 2). The anterior median fissure is filled up with dense fibrous tissue adherent to both mesial surfaces. There is no neuroglia cell proliferation to be seen in any of these areas of fibrosis, or in the white or grey matter, by either the Ranke or Cajal methods. The only glia proliferation present is in the postero-mesial column (which I have regarded as a change not dependent in any way on the obstetrical trauma because of its equal existence above, below, and at the level of the lesion) and to a slight degree in the direct pyramidal tracts. All methods used show an absence of neuroglia cells except in these two locations. The Nissl-staining characteristics of the cells and their number are dealt with under special paragraphs. The Bielchowsky fibril method shows no neurofibrils in the cells of the right sides of the cord between the fifth cervical and the first dorsal levels. The cells show no fatty change whatever by Scharlach R.

Cervical 5: The general outline of the cord on transverse section is slightly changed, the right side being somewhat smaller than the left. Both anterior horns of grey matter are distorted. The anterior horn cells are reduced in number and show varying stages of degeneration,

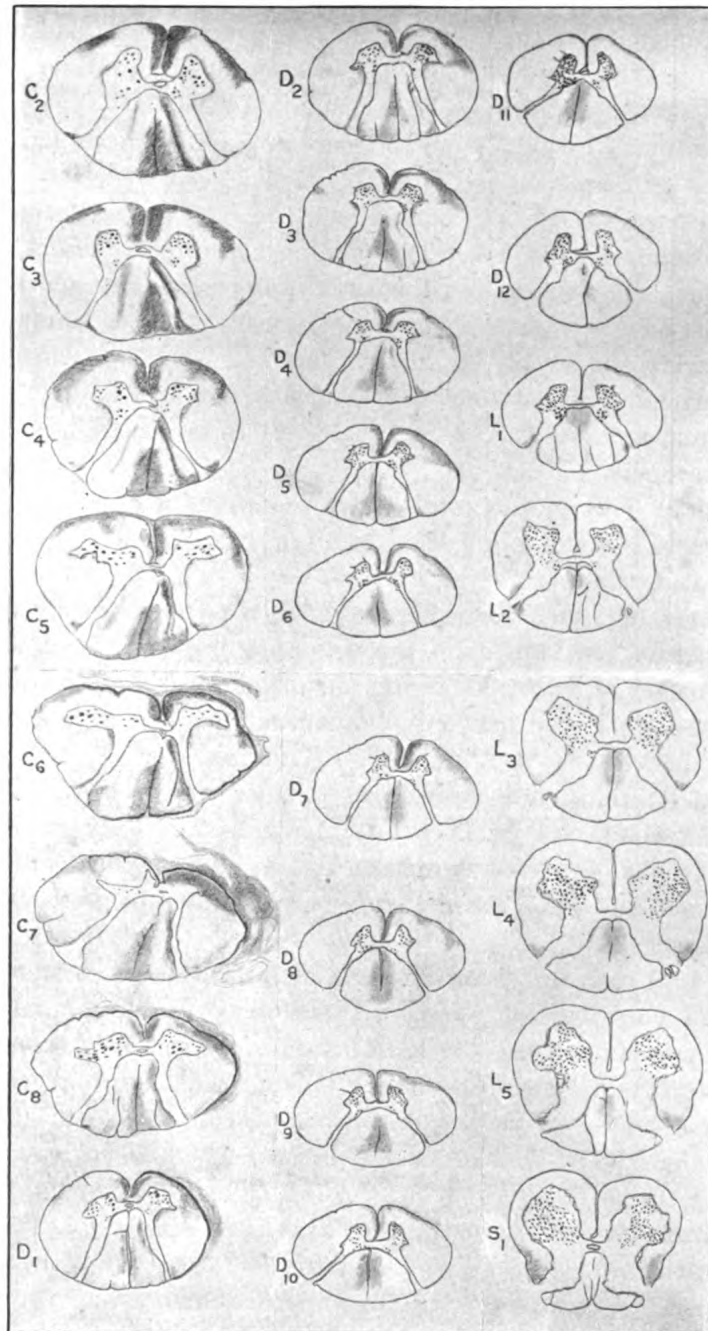


FIG. 2.

Drawing of all the levels of the cord, showing degeneration in the shaded areas (done with the Edinger projection apparatus). Approximate number and shape of the anterior horn cells shown, which were drawn in later at a magnification of 48. (Weigert-Pal.)

as evidenced by differences in size and shape, a complete absence, or a marked eccentricity of their nuclei and various stages of loss of basophilic substance, even to the condition where the protoplasm takes the basic stain evenly and intensely throughout. The cell processes are broken off in many cases. These changes are much more marked and the cells less numerous on the right side.

Cervical 6 : All conditions outlined for the level above are seen here, but to a more marked degree. The meninges are more dense, thickened and adherent. The changes in the anterior horn cells are more evident and the cells on the right side have almost disappeared, being reduced to small darkly and evenly stained cell-remains ; some having a small, dark eccentrically placed nucleus. The changes on the left side are also very great but still not as noticeable as those on the right. (See Anterior horn cells, fig. 3.)

Cervical 7 : This is the level of the maximum change. The right side of the cord is small and flattened anteriorly. The fibrosis is marked and infiltrates the peripheral part of the cord for nearly its whole circumference (fig. 4). The anterior horn zone is so involved in the sclerosis that it lies bare upon the antero-lateral surface of the cord. The grey matter of both sides is very distorted and the cells are entirely absent on the right side and only a few darkly stained elongated forms remain on the left.

Cervical 8 : The cord commences to regain a more natural shape. The meningeal fibrosis becomes less marked. The grey matter more closely approaches the normal in size and in shape. The cells are still reduced in number and marked changes are still present, but much more so on the right side.

Dorsal 1 : From this level downwards improvement is marked and rapid. The cord regains a normal outline. The peripheral fibrosis is fast disappearing at this level. The anterior horn cells resemble the normal much more closely, but are still reduced in number. Three small cells are seen in the zone of Clarke's column at this level.

Cell changes above the site of the lesion : The cells of the anterior horns above the level of the fifth cervical segment show slight general changes in some areas, but nothing to any marked degree. The nuclei are concentrically placed in the majority of them and there is no chromatolysis. Their numbers are approximately shown in fig. 2. These cells do not take a fat stain.

Cell changes below the site of the lesion : The cells in the anterior horn zone in the dorsal cord are reduced in size and show some general

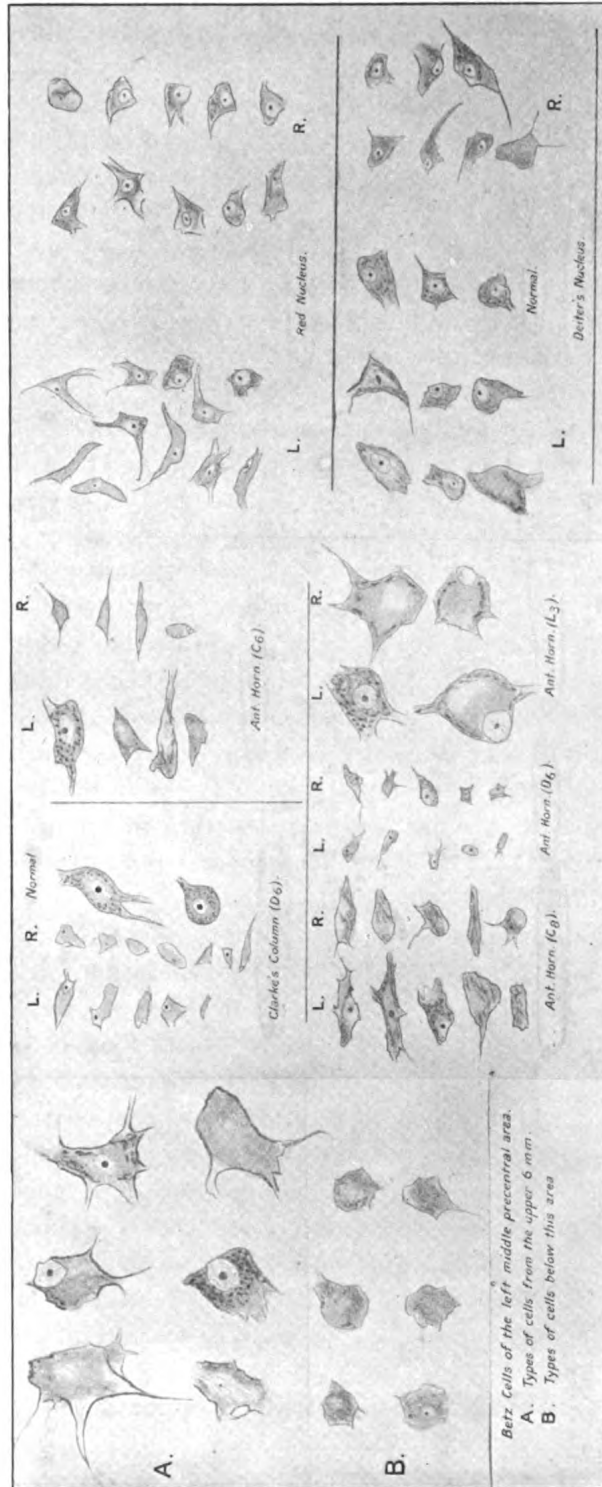


FIG. 3.
 Camera lucida drawings of cells from different areas. (Nissl.)

changes in chromatolysis. The cells of Clarke's column show great destruction, as evidenced by reduction in size, nucleolysis, chromatolysis and loss of cell processes. The changes are more marked upon the right side (fig. 3). These cells show slight fatty changes, especially on the left side. The cells of the lumbar enlargement show well-marked changes, especially on the right side at the level of the second, third and fourth segments, where they are reduced in number and show nucleolysis, eccentricity of nucleus, and chromatolysis to varying degrees. These changes no doubt have to do with the clinical phenomena in the right leg which have developed in recent years. These cells show slight staining by Scharlach R. Bielchowsky's method shows a reduced number of neurofibrils in the cells of the lumbar cord. The cells of the sacral cord are normal in number, size, and staining properties.

Descending tract changes below the seventh cervical root: Degeneration may be traced in the anterior pyramidal tract area down to the level of the eleventh dorsal segment. This degeneration is slightly more marked upon the right than upon the left side. Descending antero-lateral fibres (probably vestibulo-spinal fibres) may be traced, on the right side, down to the level of the second lumbar root. A slight antero-lateral degeneration is seen as low as the third dorsal on the left side. The location of these changes may be seen in figs. 2 and 4. A small group of fibres may be followed in the area of Schultz's comma tract as low down as the fourth dorsal root. There is no degeneration in the crossed pyramidal tract of either side except in the lower lumbar and sacral cord where there is slight change in the posterior root zone extending forward into the pyramidal tract area.

Ascending tract changes above the seventh cervical root: There is a well-marked antero-lateral ascending degeneration on the right side of the cord, and the same condition is present, but to a less degree, on the left side. These degenerated tracts may be traced into the medulla, and a well-marked bilateral degeneration may be seen in the superior cerebellar peduncles, especially that part of them adjoining the lingulæ. The inferior cerebellar peduncles show no degenerated fibres. At the entry of the posterior seventh cervical root a fibrous band takes origin, and in its ascent gradually tends towards the median line, and is last seen at the level of the second cervical segment in the posterior columns, between the lateral and mesial tracts. This degenerated fibrous band is without neuroglia cells, and is especially interesting, seeing that its posterior root ganglion is the only one (sixth and eighth cervical were not removed) that shows

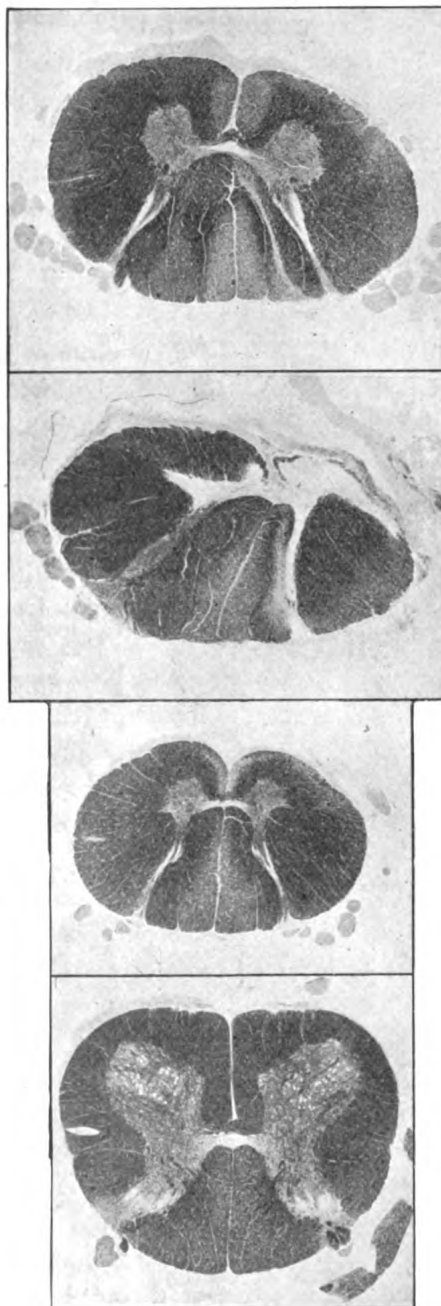


FIG. 4.

Photomicrographs of the third and seventh cervical, with the third dorsal and the fourth lumbar. (Weigert-Pal.)

degenerated fibres in it; and its cells (posterior root ganglion) are greatly reduced in number. No fibrous band can be found in the sensory tract above the posterior column nuclei. The central tract of the fillet shows a slight diffuse change. The degeneration in the postero-mesial tract has not been considered in detail, as it has no apparent connexion with the injury described. It exists far below the lesion, and, except for the additional fibrous band on the right side and a slight degree of change (apparently originating from the fifth and sixth posterior roots) in the left side, there is very little to be described in these sensory columns.

The direct pyramidal tract shows a well-circumscribed degeneration as high as the uppermost part of the cord. Unfortunately, the decussation of the pyramidal tracts was destroyed in removing the cord, but the sections of the medulla, and the pons and capsules strangely show very slight, if any, signs of degenerated fibres in the cortico-spinal system. However, the right pyramid of the medulla is smaller than the left. There is no difference in the amount of glia tissue, as shown by the Ranke method, between the pyramidal tract areas of either side.

Changes in the brachial plexus and the posterior root ganglia: The posterior ganglia of both sides of the fourth, fifth, seventh, cervical and the second dorsal roots show no changes in the number of cells, staining characteristics, or fibres; except the seventh cervical of the right side, which shows a decided reduction in the number of cells, and degenerated fibres are seen in the ganglion. The right brachial plexus is smaller, and sections show more fibrous tissue than the left. The whole of the right plexus shows a diminution in the number of nerve-fibres, and great variability in their size and depth of staining. The distribution of this degeneration is best shown by the photograph (figs. 5 and 6). The fibres in the left plexus show slight changes, especially those from the fifth, sixth and seventh cervical roots. The right and left ulnar and median nerve-bundles show no difference in the amount of perineurium or epineurium, but there is great variability in the depth of staining, and in the number and size of the individual nerve-fibrils.

Deiters's nucleus: The cells of this nucleus are less numerous on the right side than on the left. They are smaller and show marked chromatolysis, eccentricity of nucleus, or a complete nucleolysis. Some of the cells of the left side show changes, but not to the same degree as the right. Ranke's method fails to show any difference in the amount of glia between the two sides (fig. 3).

FIG. 5.

Transverse section through
cords of the left brachial
plexus. (Photomicrograph of
Weigert-Pal stained section.)

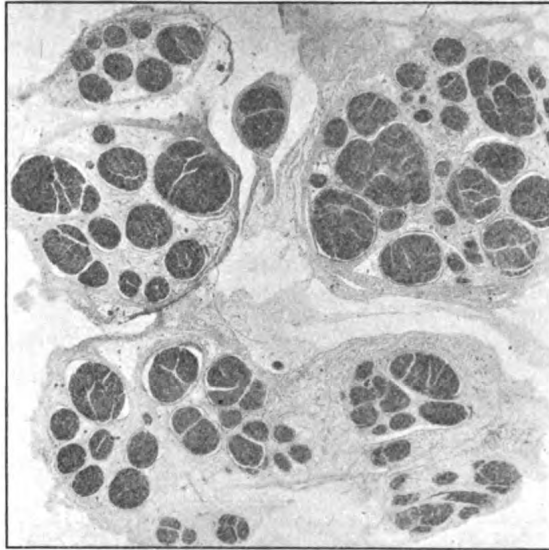
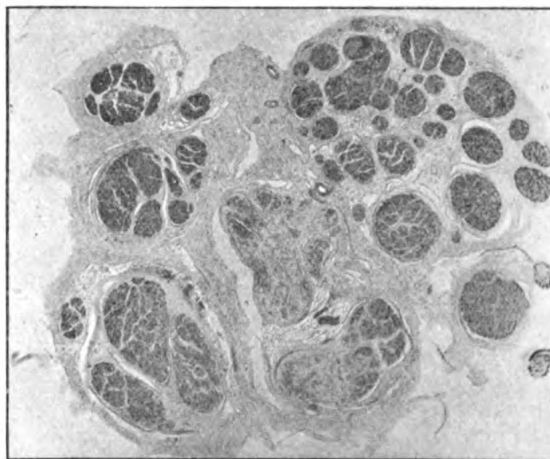
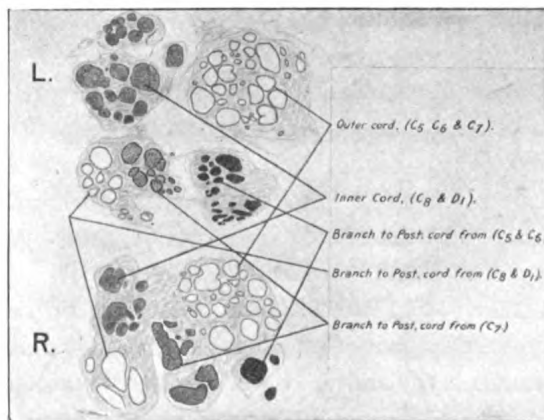


FIG. 6.

Transverse section through
cords of the right brachial
plexus. (Photomicrograph of
Weigert-Pal stained section.)



Key to figs. 5 and 6.



The red nucleus: The cells of this nucleus on the left side show more change than upon the right. The cells of the left nucleus are more elongated, their nuclei more eccentric, and the whole cell stains uniformly in intensity in many cases. No increase in neuroglia can be found on the left side (fig. 3).

The arcuate nuclei: The cells of both these nuclei are all very degenerated, showing total nucleolysis, and in many cases the cells are reduced to skeletal remains.

The cerebral arteries: The anterior, middle and posterior cerebral arteries on section show no pathological changes in any of their coats.

The cerebellum: The lobes of the cerebellum are equal in size and in general outline. The cells of Purkinje show some general change, as irregularity of outline, fracture of some of the processes, and a slight impairment in uniformity of staining. The changes are not at all confined to one side. The granular layer appears normal on both sides. There is no proliferation of glia in cerebellum, as shown by the Ranke and Cajal methods.

The Cerebrum.—The left upper precentral area: The lamination of the cerebral cortex in this area is normal, and the cells of the different layers, although slightly reduced in numbers, show no marked changes until the giant cells of Betz are reached. These cells are found only in the anterior wall of the central sulci on the external surface of the brain, but on the mesial surface they extend well forward on to the precentral gyrus. The majority of the Betz cells show various stages of degeneration. Their number is about normal. Some of the cell processes are broken off. There are various stages of perinuclear chromatolysis present. The nuclei are eccentric or absent, and the cells in a few cases are reduced to uniformly staining masses of protoplasm. Many of the cells show considerable alteration in shape, and in the periphery of some cells may be seen numerous dust-like particles, quite different in appearance from the normal basophilic granules. The majority of the cells of the precentral gyrus on the mesial surface are more globose in shape than those on the external surface, closely resembling the degenerative changes found in the right anterior cornu of the second, third and fourth levels of the lumbar cord. The Bielchowsky method shows a great reduction of the intra- and extra-cellular neurofibrils.

The cells of the intermediate precentral area are numerous, of normal lamination, and show no marked changes except that the large pyramidal layer shows slight degrees of degeneration.

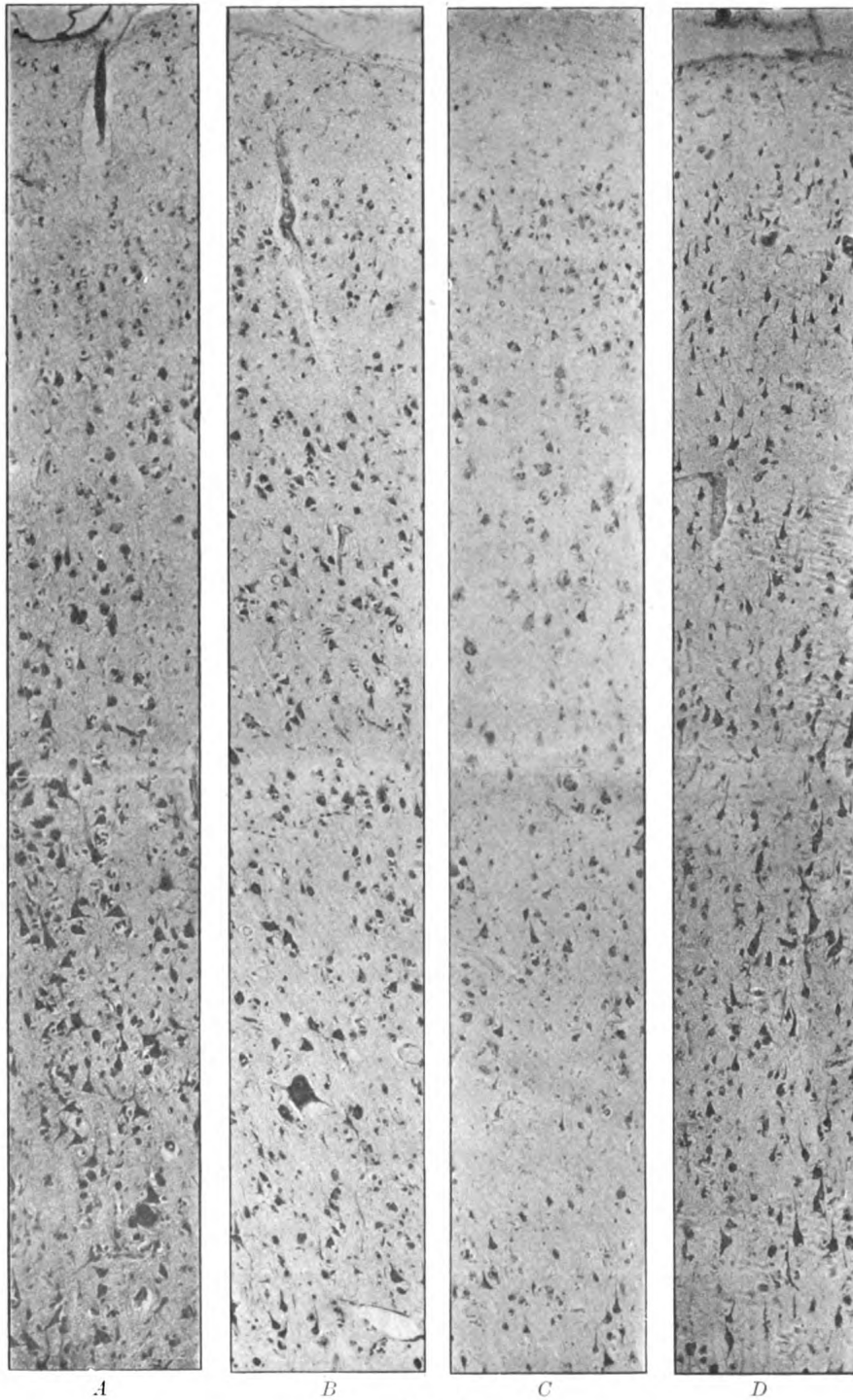


FIG. 7.

Photomicrographs of *A*, left mid-precentral area. *B*, right mid-precentral area. *C*, left intermediate precentral area. *D*, right intermediate precentral area. (Nissl, $\times 150$.)

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The post-central cortex shows no marked changes, either in lamination, number of cells, or in their staining properties.

The right upper precentral area: The cells and their lamination in this area present similar appearances to those observed in the corresponding area of the left side, but the Betz cells do not show the same degree of change. The intra- and extra-cellular neurofibrils are more numerous than on the left side.

The cells of the intermediate precentral area are about normal in number, shape and size. The cell lamination of the cortex in this area is of normal appearance.

The cells of the post-central region show no special changes.

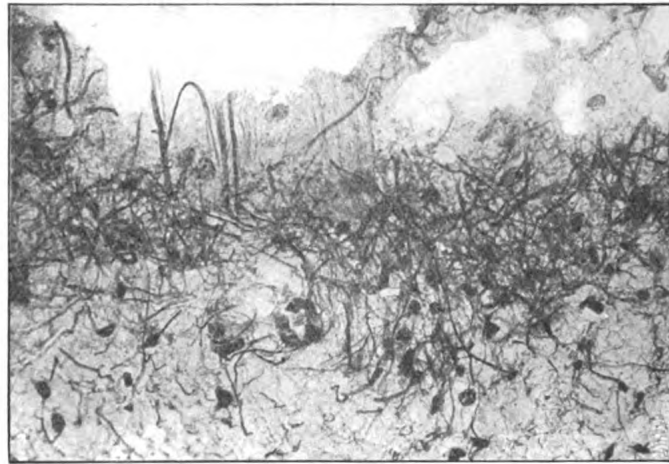


FIG. 8.

Photomicrograph showing sub-pial felting due to glia proliferation in the tangential layer of the left middle precentral area. (Ranke, $\times 350$.)

The left middle precentral area: The cells in this area (and more especially those of the superficial pyramidal layers) show more general changes, but no reduction in number when compared with the cells of the corresponding area of the opposite side (fig. 7, A). The degenerative changes are especially marked in the Betz cells. These latter cells in about the upper 6 mm. of the area (i.e., the 6 mm. immediately below the superior genu) are of the types represented in the first two upper rows of fig. 3. Here is seen loss of cell processes, eccentricity or absence of nucleus, and chromatolysis. There is scarcely one cell in this area that might be called normal. Below this, over an area

of about 4 to 6 mm., the giant cells are greatly reduced in number, and are small, darkly stained bodies, devoid of processes, and without any trace of nucleus, nucleolus, or basophilic granules (fig. 3). Over the remainder of the area the Betz cells have almost disappeared, only occasionally a cell of the type last mentioned may be found. The cells of the polymorphous layer show slight general changes. The Bielchowsky method shows few neurofibrils in this area, and the giant cells stain very badly. Scharlach R does not stain any of the cells of this area. The neuroglial changes here are very definite.

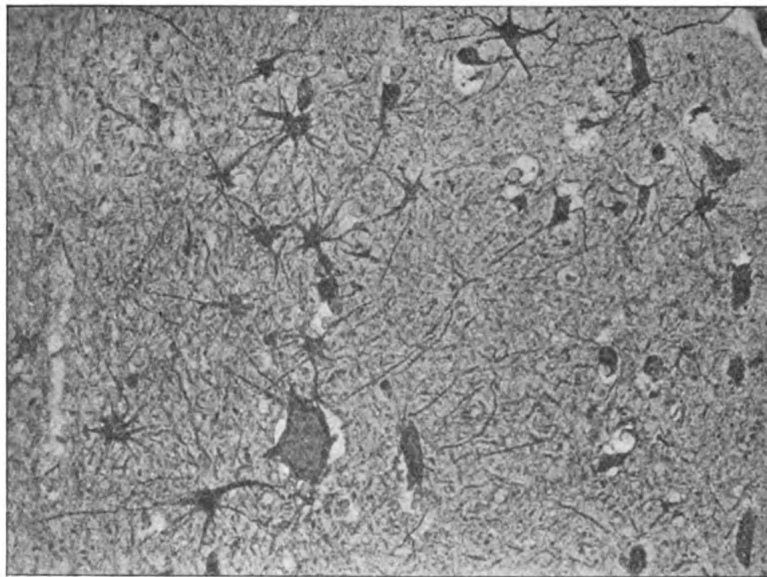


FIG. 9.

Photomicrograph showing proliferation of glia cells around a small vessel in the polymorphous layer of the left middle precentral area. (Cajal, $\times 400$.)

Whilst there are some changes in the corresponding area of the right hemisphere, the densest neuroglial proliferation is seen in the left precentral area, and only here are the changes definite and constant. The proliferation of neuroglia in the tangential layer is very evident, as can be seen as a dense sub-pial felting by reference to fig. 8. There is no demonstrable proliferation of glia below the molecular layer until the Betz cell layer is reached. Below this area, in the polymorphous layer and in the cortico-medullary area, the glia tissue is much proliferated (*see* fig. 9, showing proliferation around a vessel).

Hence the glia is laminated in the deeper layers, and especially so in the polymorphous layer. This proliferation of glia is very similar in distribution to that shown by Dr. Mott in "Amyotrophic Lateral Sclerosis" [15], where he described the deeper layers of the motor cortex alone involved in the gliosis.

The intermediate precentral area of the left middle motor cortex (*see* fig. 7, C) shows a very great general reduction in the number of cells, and especially so in the medium-sized and in the large superficial and deep pyramidal layers. These profound changes are found only in the intermediate precentral, are as outlined by Campbell [5], and do not extend forward on to the frontal convolutions. The cells of

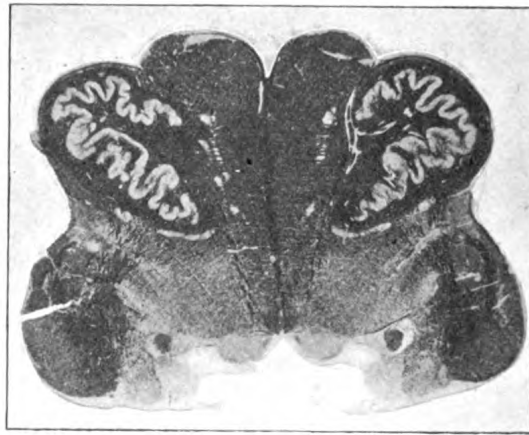


FIG. 10.

Photomicrograph of a transverse section through the middle of the olives.
(Weigert-Pal.)

the large superficial pyramidal layer show the greatest change, there being complete chromatolysis and very frequently nucleolysis. The cell processes are broken off, and in some cases the cells are reduced to skeletal remains. The most severe changes in this area of the cortex are seen in the large pyramidal layers. The internal large pyramidal layer shows cells in the late stages of degeneration.

The post-central area of the left middle cortex shows very little general change, and in no detail differs from the post-central cortex of other areas.

The fibre system of the left middle precentral area shows very general and decided changes when compared with the same area of the right hemisphere. The plexiform, supra-radiary, and radiary fibres

of the left side have almost totally disappeared. The fibre system of the right middle motor area presents a totally different appearance. The plexiform layer is the only one that shows any degree of change in this area, and here the fibres are delicate and scarce. The supra-radiary and radiary fibres are much nearer to the normal both as regards appearance and numbers. These changes in the cortical fibre system are relatively more marked than the cell changes.

The corpus callosum shows some scattered areas of secondary sclerosis, especially in its middle one-third. The genu and the splenium cut and stained in the same celloidin block show no such degenerative change.

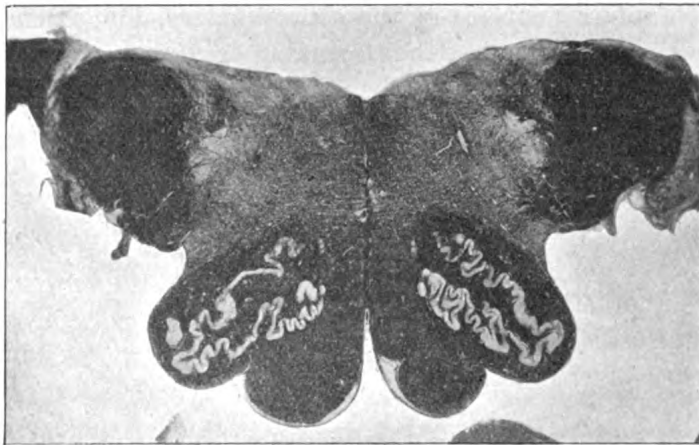


FIG. 11.

Photomicrograph of transverse section through the uppermost parts of the olives. (Weigert-Pal.)

The right middle precentral area: The lamination of this area is normal, but the cells show some general change although not to the same degree as the left side (fig. 7, *B*). The Betz cells vary in appearance, but the types are different from those on the opposite side, in that the chromatolysis is not as marked and there is not such complete nucleolysis. The number of Betz cells is somewhat below the average. The Bielchowsky method shows a reduced number of intra- and extra-cellular neurofibrils as compared with the normal, but a great increase over its fellow of the opposite side. The Ranke method shows no proliferation of glia in the tangential layer, nor is there the same proliferation of glia in the deep layers of the precentral area.

The intermediate precentral area is well laminated. The cells here

are much more numerous. Their cortical processes point perpendicularly to the molecular layer, and there is no degree of fragmentation of the cells themselves. This condition is maintained generally throughout the area, and stands out in marked contrast with the corresponding area of the left hemisphere (fig. 7, D).

The post-central area of this side shows no distinctive changes from the same location in the left post-central cortex.

The right and left lower precentral areas: The changes in the face areas of both hemispheres will be described together as the conditions found coincide. The number of cells and their lamination show no marked changes from the normal. The giant cells are smaller than those in the other areas, and do not confine themselves only to the anterior surface of the central sulcus, but extend forward on to the external surface of the ascending frontal convolution. They are very much less numerous than in other areas, and at the lower end of the sulcus none can be found. The chief changes in the Betz cells are some chromatolysis and eccentricity of nucleus with no nucleolysis, but there is a noticeable absence of the other extensive changes which were described in the left arm and leg areas. There is no proliferation of glia to be found in the plexiform or deep layers on either side.

The intermediate precentral and the post-central areas of both sides show no special changes.

LITERATURE.

With the exception of papers describing the ordinary type of brachial plexus root lesions, the literature relating to the pathological changes found in obstetrical paralysis is very scanty. Numerous cases have been reported from the clinical and surgical aspects, with occasionally a short outline of the pathological condition present, which is usually in the fifth cervical root near its junction with the sixth. But more roots than the fifth are often involved. Occasional mention is made of injury to the cord, but with no great detail. The present case is therefore of more than usual interest as the local and general changes of the cerebrospinal system have been described.

The more severe cases reported usually have a history of difficult labour and asphyxia. Huet [12] describes a case with version and double upper arm paralysis, probably from extension of the arms over the head. Babonneix [1], Raymond [20], Thomas [22], and Broca [3], record cases where resuscitation was especially difficult. This may

be the result of interference with the neighbouring nuclei of the phrenic nerve from hæmorrhage or trauma of the cord, or it may be from pressure of the phrenic nerve itself, or it may perhaps be explained by the shock of the injury, especially when much hæmorrhage is present, or it again may be due to exhaustion from the difficult prolonged labour alone. One or all of these conditions may help to explain the asphyxia found in this type of case.

The ætiology of this lesion is generally ascribed to a pathological increase in the distance between the tip of the shoulder and the head in delivery. Bailey [2] fixes thirty degrees as the limit for the axis of the head to be drawn laterally away from the long axis of the body without danger of the cords being stretched severely or ruptured. Carter [6] mentions stretching or rupture of the upper roots of the brachial plexus during the process of delivery as the only cause of this condition. There are various other views, such as pressure with the forceps, pressure on the first rib or over the transverse process of the vertebræ, and pressure by the scapula.

I have exposed by careful dissection four brachial plexuses in newly born infants, and have found that if forcible traction is exerted in a downward direction the fifth and sixth cervical roots are most stretched, but if the traction is exerted in a line at right angles to the mid-line of the body, the middle cords of the roots of the brachial are the first to become taut. If great traction is exerted on the arm in a line at right angles to the body I have produced in the cord an evulsion from the cord substance of the anterior and the posterior nerve-roots, and this is most marked in the seventh and eighth cervical levels. The peripheral part of the nerve-roots is materially stretched, but I could find no microscopic evidences of fragmentation of the fibres. Traction in this line may explain the condition and the roots involved in this case. But as can be readily understood, traction in this line (right angles to the body) does not seem, from a physiological point of view, to be of any assistance in labour.

Clark, Taylor, and Prout [7], in their exhaustive paper report only one case of rupture of all the roots, and the only pathological lesions mentioned are rupture of the perineural sheath with coincident hæmorrhage and laceration of the nerve-fibrils of the brachial radicals. They comment on the slight sensory changes found in these cases, and upon the resultant traumatic neuritis sometimes seen clinically. Prout [19], in his article upon the pathology, only mentions again the presence of rupture, hæmorrhage and laceration of the nerve-bundles. Weil [24],

from the clinical standpoint, describes three types—viz., the upper arm, the lower arm, and the mixed types—and he describes a case of lesion of the entire plexus. Warrington and Jones [23] state that sensory changes are especially liable to be found in cases where the lower radicals of the plexus are torn, and they place the lesion as intra-, inter-, or extra-vertebral. Oppenheim, in his text-book on Nervous Diseases, states that Bruns believes that the effect of traction often extends into the cord itself, and that this accounts for some of the unfavourable cases. Oppenheim, however, chiefly considers peripheral root lesions. Burr [4] suggests the cord as the site of the lesion much more commonly than is generally accepted. Gallavardin [8] reports a case with very slight motor lesions, but marked sensory changes over the whole of the upper limb. Raymond's [20] case had double upper arm paralysis and a spastic gait, which he concludes was due to hæmatomyelia and interference with the pyramidal tracts. Neurath [17] speaks of cord lesions in obstetrical paralysis, and found multiple miliary hæmorrhage in the lumbar cord in a case dying shortly after birth. Jolly [13] reports a case of bilateral paralysis of the lower arm type specially involving the seventh cervical root. Thomas [22] mentions a case with rupture of the cord and meninges between the sixth and seventh cervical roots in a footling presentation. Gott [9] reports three cases with autopsies showing hæmorrhages into the lumbar cord in foot presentations. These cases had sensory changes. Gravellona [10] states that obstetrical lesions may involve the brachial plexus or the cord, and he reports a case followed by Little's syndrome. Philippe and Cestan [18] report a very interesting case with coincident spastic gait, which they, however, show to be due to a cortical lesion and not to interference with the pyramidal tracts. The child died of scarlet fever at the age of 6, and they found a brachial plexus lesion very similar to that described in this case with a cervical pachymeningitis, and the posterior root fibres were more involved than the anterior. They describe degeneration in the antero-lateral tract of the cord descending to the tenth dorsal root; also pyramidal tract and posterior column degeneration. Although the sensory root fasciculi were much damaged, they described no sensory changes. They found no signs of hæmatomyelia, and described a true cicatricial organization around the bundles of the brachial plexus, and a great reduction in the number of nerve-fibrils. The chief lesion was at the level of the eighth cervical root. There was no oculo-pupillary disturbance.

The case which forms the subject of this paper presents several

points of interest. Unfortunately I have been unable to obtain a detailed account of the clinical and electrical examination of the upper and lower limbs of the right side, but in the case of the latter the history clearly shows that the paresis is of comparatively very recent development.

SUMMARY.

(1) The seventh cervical root, which is the site of greatest trauma in this case, is not the usual point of maximum lesion as described in the great majority of cases of obstetrical paralysis.

(2) The usual site of the lesion is the nerve-trunk itself, but in this case there was superadded a more grave injury of the cord amounting to a Gudden's evulsion at the level of the seventh cervical root, and diminishing in severity above and below this point.

(3) Although the left arm was not involved at labour, yet histological examination shows that there was great cell destruction on that side in the cord, especially at the seventh cervical level.

(4) The sensory system in this case suffered least damage. The fibrotic band which originates at the seventh cervical root of the right side is found to disappear at the nuclei of the posterior columns (i.e., it is not seen in the medulla or pons).

(5) The local fibrosis can be best explained by the invasion of an organized fibrous tissue, resulting from the trauma, into the injured areas of the cord. The almost complete absence of glia cells locally is very definite and is rather difficult to explain, seeing that in this case much more than the meninges and peripheral roots were injured.

(6) It is difficult to explain the well-marked changes in the direct pyramidal tracts in the cord and the absence of degeneration (to any corresponding degree) in the medulla or pons (compare figs. 4, 10, and 11). The explanation may possibly be found in the fact that the pyramidal tracts are not myelinated at birth, and the sclerosis in the area of the direct pyramidal tracts in the spinal cord may be an irritation phenomenon of a local nature as the results of the trauma, but the axons above the local field of injury corresponding to their systems not being myelinated and consisting only of delicate protoplasmic strands, might conceivably disappear without leaving any appreciable tracts of sclerosis amidst the abundant myelinated fibres constituting the pyramids. On these grounds alone, however, it is difficult to explain why the degeneration in the area of the direct pyramidal tracts descends so far below the local traumatism. The above explanation may also apply to the absence of degeneration in the right crossed pyramidal

tracts; these being so deeply placed and not having suffered any local injury, the axons for the right upper limb have disappeared and leave no demonstrable remains. Or Kapper's work on Neurobiotaxis might suggest an explanation, in that the axons may not have been attracted to the anterior horn cells at the site of the trauma, owing to their great impairment of function or total destruction. Although there is a great difference between the size of the right and left crossed cortico-spinal tracts, yet up to very recent years this right crossed tract for the leg has functionated perfectly; and there is no evidence from the condition of the fibres below the lesion in the cervical area that the tract was implicated in the local process. This suggests that a physiologically functioning system of fibres is not invaded or strangled by glia or fibrous tissue in process of proliferation or cicatrization, which has likewise been shown experimentally in monkeys not to occur [16].

(7) The changes in Deiters's nuclei on either side indicate some involvement of the vestibulo-spinal system of fibres. This is especially well marked on the right side.

(8) The scarcity of cells and the degeneration in the red nucleus, especially on the left side, rather suggest that some interference with the right rubro-spinal tract has taken place which may perhaps be located in the region of the much injured anterior horn of grey matter at the level of cervical 7. These changes are in distinct contrast to the absence of changes in the cerebellar cortex.

(9) Unfortunately there is some general change in the giant cells of the cerebral motor cortex, but examination of the left middle motor area in its middle and lower parts clearly shows the almost total destruction and disappearance of the Betz cells. Some of this cell degeneration closely resembles that described in cases of amputation recorded by Campbell [5]. This is especially striking in the small and darkly stained masses without processes or nuclei. I am unable to report the complete disappearance of all the Betz cells as Gordon Holmes and Page May [11] have described after 229 days in their experimental work on the localization of the motor areas. Sewell and Turnbull [21] found no marked reduction in the number of Betz cells, but a general degeneration of them fifty-six days after an accident causing a complete transverse lesion of the cord in the cervical region.

(10) The cell destruction of the intermediate precentral area of the middle motor cortex of the left side is seen throughout the area and is most striking. The magnitude of the changes in this area

would seem strongly to suggest that it has to deal pre-eminently with the motion of the upper limb. This area, and especially the large pyramidal cells, may be (as Brodmann suggests) merely the seat of the ideation of movement, or perhaps (combined with that function) it is the centre for the more delicate and skilled manipulations of the upper limb, leaving the more gross movements to the Betz cells.

(11) The post-central cortex has no local changes referable to any one particular area.

(12) The marked changes in the fibre system of the left middle precentral cortex strongly substantiate the importance of the degenerative phenomena described in the Betz cells of this area.

(13) The glial changes in the left middle precentral area are constant in two localities. In the tangential layer the sections show varying amounts of glia proliferation and a more constant change is seen in the deep layers of the cerebral cells where the glia tends to distinct lamination.

(14) The right leg atrophy I can in no way correlate satisfactorily with the changes described as due to the obstetrical trauma. The history is very definite as to the absence of any clinical phenomena in the leg until comparatively recently. It appears to be a primary degeneration of the cells in the anterior horn of grey matter in the lumbar enlargement of the cord, and associated with it a similar degeneration in the Betz cells in the left upper precentral area without any demonstrable degeneration in the right crossed pyramidal tract.

(15) It is highly improbable that excision of part of the nerve-trunk and anastomosis of the two ends as Kennedy [14] suggests and practises would be of any avail in obstetrical paralysis of the severity of this case, and almost assuredly the operation would be followed by disappointing results. Fortunately cases of this malady are not frequently seen in such severe forms and in the same location as the one I have just described; but this case and a review of the literature suggests to one that in severe and persistent cases of paralysis resulting from obstetrical trauma, the probability is that the cord is injured much more frequently than is generally considered. The greater part of the literature relates to the clinical and surgical aspects of the condition, while that dealing with the pathological changes, in the majority of cases, only makes mention of laceration of the nerve-fibres and sheaths in their radicals without any consideration of the possibilities of medullary lesions of the cord.

In conclusion, I wish to thank Mr. Charles Geary for the photographs.

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The Changes in the Central Nervous System resulting from Thyro-parathyroidectomy.

By WALTER EDMUNDS, F.R.C.S.

THE effects produced on the nervous system by the excision of the thyroid and parathyroid have been described by various observers. In 1902 I communicated to the Pathological Society a paper on the effects produced by thyroid excision and by thyroid feeding [1]. The experiments there related included three in dogs in which thyro-parathyroidectomy had been performed. These three dogs died, or were killed because they were about to die, one in three, one in six, and one in twelve days. This is the usual result of this operation, for under usual conditions carnivora generally die a few days after the operation, only about 4 per cent. surviving. It has, however, been pointed out by W. G. MacCallum and Voegtlin [3] and others that if these dogs are treated with calcium salts in large doses a considerable number of the animals will survive the operation, with or without symptoms during the first few days. Experiments to test this have been performed by myself both on dogs and cats and the results published [2]; in dogs there was a recovery of 45 per cent., and a similarly good result was obtained in cats, the animals surviving many months. These results were obtained by giving calcium as lactate, either by the mouth or intravenously, or by feeding the animals with milk (which contains much calcium).

On the previous occasion the experiments were made at the Brown Institution, and the nervous systems of the animals were, by kind permission of Dr. Mott, examined at the Pathological Laboratory of Claybury Asylum, and the same has been done on the present occasion. Although the animals when treated with calcium survive the

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operation several months, they do eventually die as a result of it. Of the three animals in which the changes about to be described occurred, the two cats survived seven months each and the dog four and a half months. I have at the present time a dog living on milk and in good health which was operated on thirteen months ago.

The dog whose nervous system was examined was fed on milk, a quart a day, and was given in addition 30 gr. (2 grm.) of lactate of calcium a day; then it was submitted to total excision of the thyroid and parathyroids. The day but one after the operation the dog had severe tremors; 9 gr. (0.6 grm.) of lactate of calcium were given intravenously. The next day the dog was nearly well; he was running about and seemed quite bright. He continued well (on milk diet) for four months and eleven days after the operation, then the gait was affected and the hind limbs seemed stiff; there was no sugar in the urine. The next day the dog seemed dull, ran about only slowly, and could not jump up on his hind legs. Two days later the dog died. The post-mortem, which was made about three hours after death, did not show any changes to the naked eye; the brain and cord were put into a 5 per cent. formalin solution.

Cat No. 1.—This cat was fed on normal goat's milk; it then underwent total excision of the thyroid and parathyroids, and did well for two months, when it had an attack in which it seemed stupefied and breathed rapidly; there was no sugar in the urine. From this attack the cat recovered and remained well till seven months after the operation; the animal then had an altered gait and walked with its legs apart. The next day the animal was worse and could hardly stand, and was destroyed by chloroform; the brain and cord were at once removed and placed in a 5 per cent. formalin solution.

Cat No. 2.—The cat was fed for some days on milk only; it was then subjected to total excision of the thyroid and parathyroids; it was then given, in addition to the milk, 30 gr. a day of lactate of calcium. The cat had no symptoms, except that in four months' time it was thought to be somewhat thin. Six months after operation the cat had an attack in which it seemed very dull and did not take its milk properly; the attack passed off and the cat remained fairly well for a month, when it had another similar attack; there were no tremors on either occasion. The next day the cat, being no better, was destroyed by chloroform; the brain and cord were at once taken out and placed in a 5 per cent. formalin solution.

It will be noticed that the two cats were destroyed by chloroform;

they did not require much, as they were very ill at the time. In order to avoid any source of fallacy arising from this, a normal cat was killed by chloroform and its brain and cord treated in the same way and used for comparison. The dog died of the symptoms.

After hardening, the portions were embedded in paraffin and cut. The changes about to be described were shown by staining by the Nissl method; sections were also stained by the Ranke method, but they showed no glial proliferation; also by the Weigert-Pal method, but they showed no tract degeneration, also those stained by the Marchi method did not show any fatty degeneration.

DESCRIPTION OF SPECIMENS.

Cat No. 1.—Spinal cord: The changes are most marked in the medium-sized and smaller cells; in many of these the body is partly or wholly destroyed. In the cell drawn it will be seen that the Nissl bodies are undergoing chromatolysis: the nucleus is destroyed and the cell is invaded by satellite cells, which are seen in the body of the cell; the upper cell is not so far advanced towards destruction. Medulla: Changes similar to those in the spinal cord are found in all the cells of the medulla, though not so marked. Cerebellum: The cells of Purkinje also show changes similar to those found in the cord. Cortex: The medium and large pyramidal cells exhibit the following changes: in many the Nissl bodies are undergoing chromatolysis, while many others are utterly destroyed, only the outline of the cell being visible; many of them are being invaded by satellite cells.

Cat No. 2.—Spinal cord: Shows similar changes to those described in Cat No. 1 (*see fig. 1*). Medulla: Shows similar changes in its cells (*see fig. 2*). Cerebellum: The cells of Purkinje are seen in all stages of destruction. Cortex: Similar changes to those found in Cat No. 1. The pituitary body was examined, but no changes found.

Dog No. 1.—Spinal cord: The cells, both large and small, are affected, the changes being even more marked than in the cats; many of the cells are nearly totally destroyed and quite past regeneration. Many of the cells are far more destroyed than those shown in the drawings, which represent an average group. Medulla: There are some changes, but they are not so advanced as those seen in the cord. Cerebellum: There are the same changes as those described in the cells of Purkinje in the cat. Cortex: Cell body is swollen; the Nissl bodies are undergoing chromatolysis; in some cells the nucleus and nucleolus

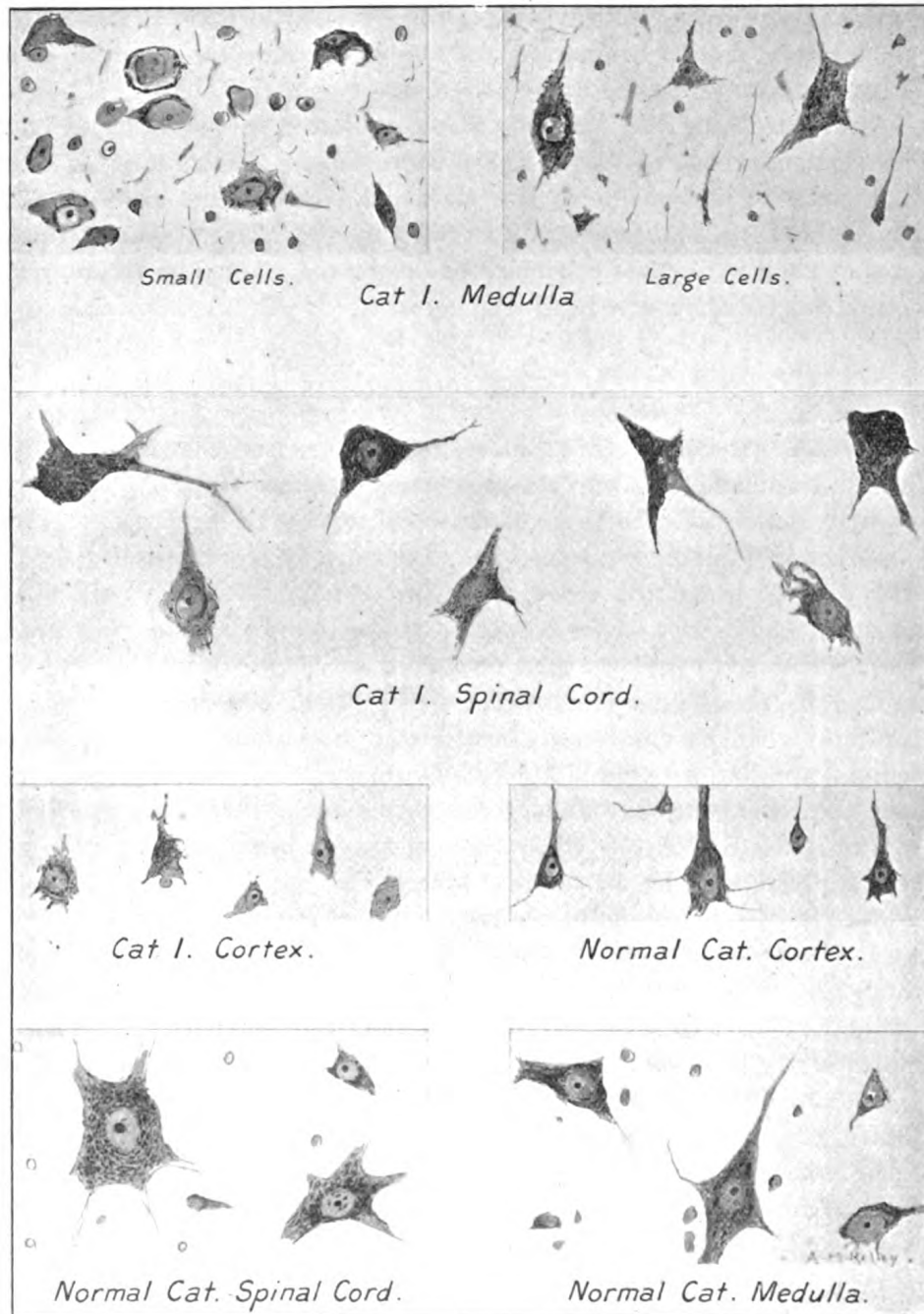


FIG. 1.

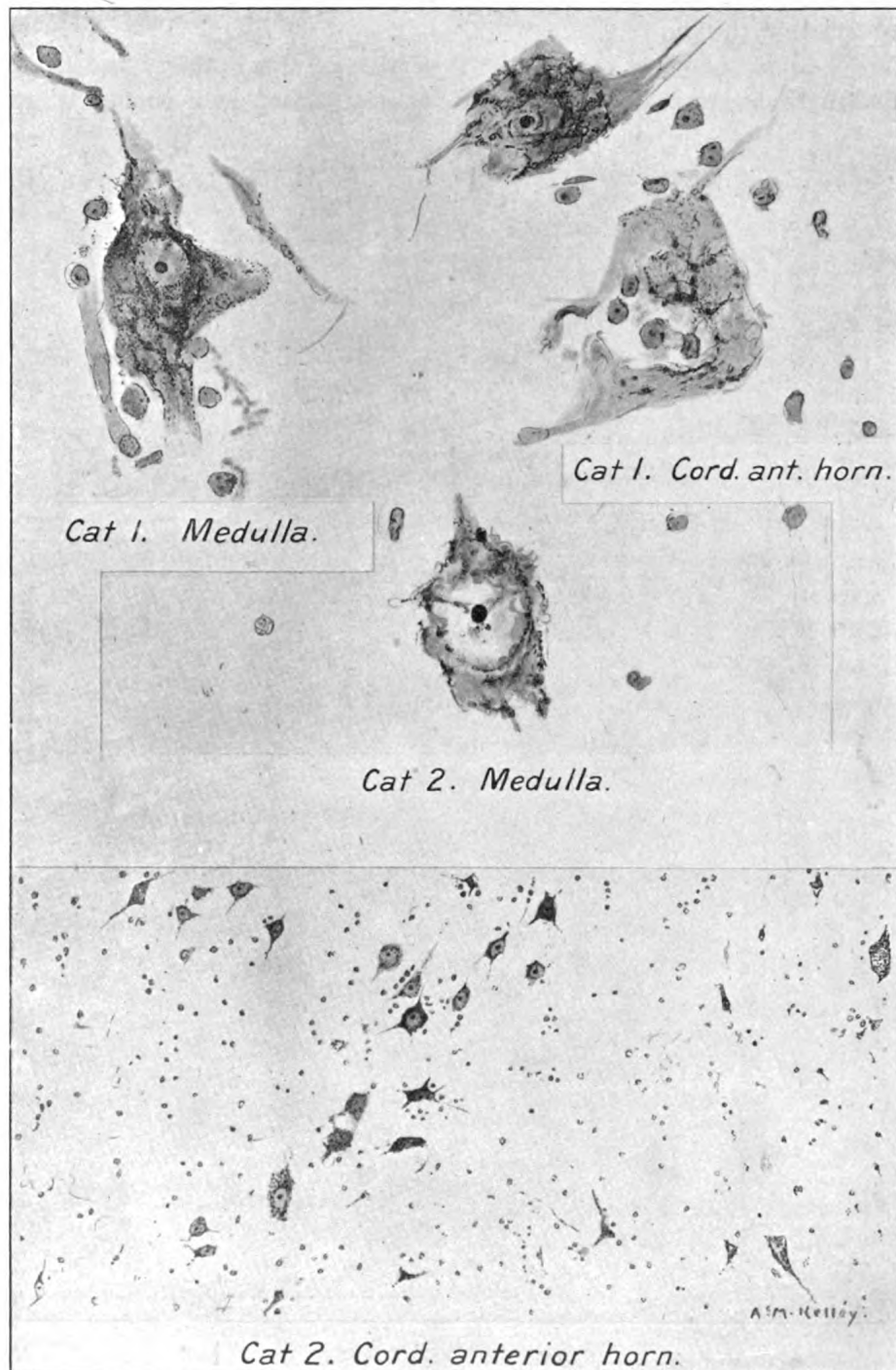


FIG. 2.

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have disappeared, as shown in the drawings. Pituitary: No change can be detected (*see* fig. 3).

The percentage of calcium in a portion of the brain of the thyro-parathyroidectomized dog, and also for comparison in a portion of the

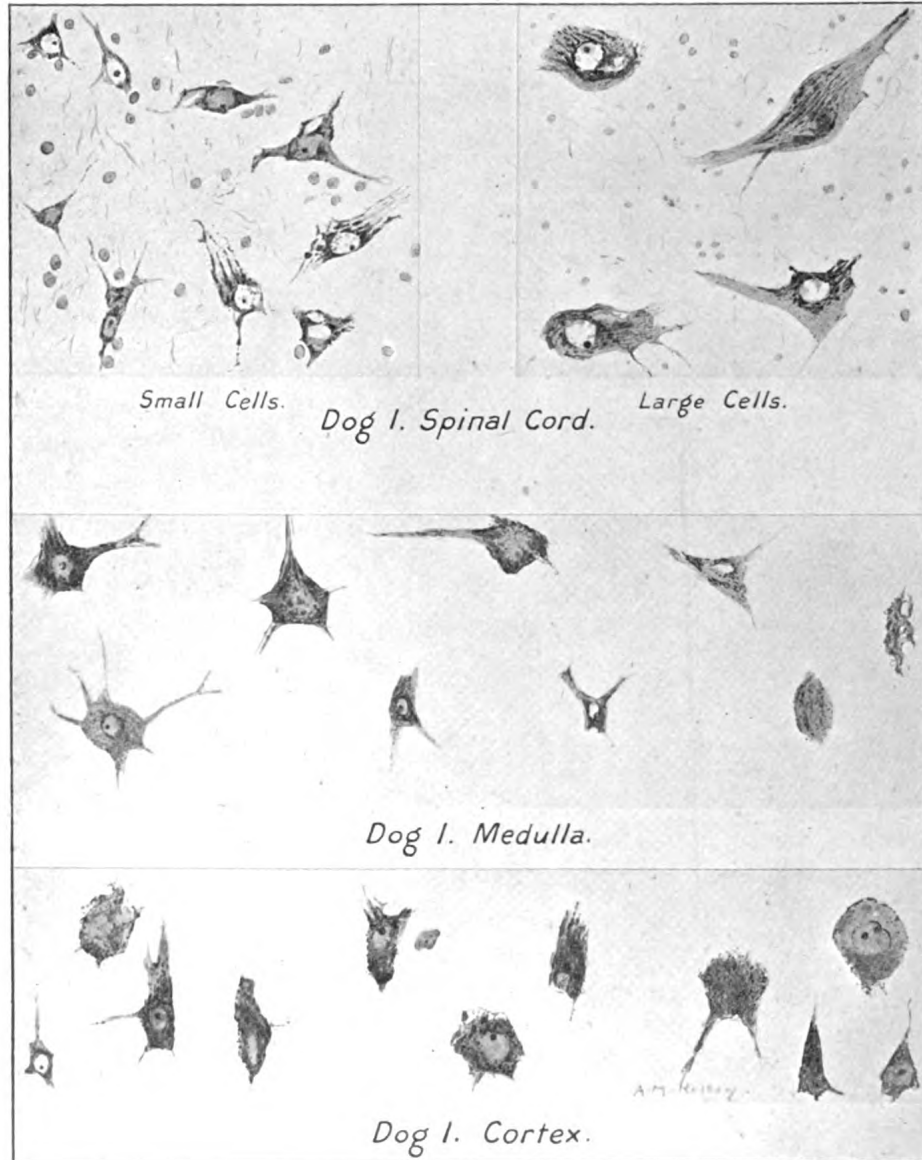


FIG. 3.

brain of a normal dog, was kindly determined by Mr. Mann, the chemist at Claybury. He found as follows:—

NORMAL DOG'S BRAIN.

Reduced to ash	0.2376 grm. ash
From which	0.0036 „ CaO
					= 1.5 per cent. of CaO in ash

THYRO-PARATHYROIDECTOMIZED DOG.

Reduced to ash	0.2192 grm. ash
From which	0.0015 „ CaO
					= 0.7 per cent. of CaO in ash

This reduction of calcium to a half in the brain of the operated dog agrees with the result obtained by MacCallum and Voegtlin: they also found a marked diminution in the amount of calcium in the blood of a parathyroidless dog. They consider that the removal of the parathyroids leads to a drain of calcium from the system, and that this can be remedied by the administration of calcium; the experiments here related go to confirm that view.

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